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XXIV. A. ACTION OF EPINEPHRINE ON PIAL VESSELS; B. ACTION OF PITUITARY AND PITRESSIN ON PIAL VESSELS; C. VASOMOTOR RESPONSE IN THE PIA AND IN THE SKIN

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A. ACTION OF EPINEPHRINE ON PIAL VESSELS

Since the publication in 1928 of a paper from this laboratory on the vasomotor control of the cerebral vessels[1] with a preliminary description of the effect of epinephrine on the arteries in the pia-arachnoid, several facts have come to light which make it desirable to review critically our earlier findings. These facts have been secured partly through our own recent work and partly through that of others.

In 1931, Riser, Mériel and Planques,[2] studying the pial vessels in dogs and cats through a cranial window such as we have used, concluded that intravenous and intracarotid injections of epinephrine in various dosage caused dilatation of the arteries in the pia. Occasional exceptions to this response were noticed. The local application of epinephrine to the surface of the brain caused constrictions (or "slight diminutions in caliber" as the authors preferred to term them) of from 10 to 18 per cent in about one third of the cases, but no dilatations. They found that the constrictions caused by epinephrine (locally applied) could be overcome and converted to dilatations by raising the blood pressure abruptly with the intravenous injection of ephedrine or epinephrine.[3] The striking point to these workers was the absence of intense spasm in pial arteries compared with that seen in arteries elsewhere. This will be referred to again in part C. They pointed out,

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1. Forbes, H. S., and Wolff, H. G.: Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

2. Riser, Mériel and Planques: Encéphale **26**:501 (July-Aug.) 1931.

3. We have verified this observation (see the experiment described on pages 975 and 976, part C).

also, that the absence of spasm of the pial arteries from epinephrine contrasted strongly with the presence of intense spasm when the walls of the vessels were stimulated by mechanical, chemical or electrical means. Riser's results are not set down in tabular form, and the actual figures are not always stated, but merely indicated by the text. In table 1 we have interpreted the latter as accurately as we were able.

Recently, Franke and Seager,[4] studying the pial arteries of dogs by similar methods, obtained a somewhat higher percentage of constrictions

TABLE 1.—*Riser's Findings*

Type of Injection of Epinephrine	Dosage	Strength of Solution	Animals	Trials in Which Pial Arteries Showed: Constriction	Trials in Which Pial Arteries Showed: Dilatation	Trials in Which Pial Arteries Showed: No Change or Changes of Less Than 10%	Instances in Which No Changes Were Mentioned	Total Number of Trials
Local.....	0.1-0.01 Mg. per Kg.	"Stronger"	.....	7	0	0	—	7
		"Weaker"	.....	0	0	13	—	13
Intravenous	1-0.01 Mg.*	.....	Dogs	6†	10‡	—	2	18
			Dogs	0	25‡	—	—	25
Intracarotid	0.1-0.00002 Mg. per Kg.	.....	Cats	2‡	—	5	5	12

* Doses of 0.000002 mg. were said to give similar results. There is perhaps some mistake or misunderstanding in regard to these figures, since any dose less than 0.0002 mg. is beyond physiologic range.
† Animals' condition poor; low blood pressure.
‡ Animals' condition good.

TABLE 2.—*Results of Experiments on Thirteen Cats and One Monkey*

Type of Injection of Epinephrine	Trials in Which Pial Arteries Showed: Constriction	Trials in Which Pial Arteries Showed: Dilatation	Trials in Which Pial Arteries Showed: Dilatation Followed by Constriction	Total Number of Trials
Local.....	9	0	3	12
Intravenous.....	0	2	4	6
Intracarotid.....	3	0	0	3

after both local and intravascular injections than Riser did, but qualitatively the results were similar. Additional experiments [5] of our own with cats showed that intravenous injection of epinephrine caused dilatation in the vast majority of cases, and that intracarotid injection, contrary to our previous findings, caused dilatation more often than constriction.

The preliminary findings with thirteen cats and one monkey (published in our earlier paper [1]) are given in table 2. From 0.5 to 1 cc. of

4. Franke, F. E., and Seager, L. D., St. Louis University School of Medicine: Personal communication to the authors.

5. The experiments referred to were carried out before we knew of Riser's work.

dilutions of epinephrine of from 1 : 10,000 to 1 : 500,000 in Ringer's solution was given.

EXPERIMENTAL OBSERVATIONS

We have completed a new series of experiments (on forty-seven cats and four monkeys) with epinephrine,[6] using a cranial window and essentially the same technic as before.[1] Amytal and dial[7] were the anesthetics except in one instance, in which ether and morphine were used. The results have been divided into three groups.

TABLE 3.—*Results of Experiments on Forty-Seven Cats and Four Monkeys*

Dilution of Epinephrine	Site of Injection	Number of Trials in Which Pial Arteries Showed: Constriction	Dilatation	Dilatation Followed by Constriction	No Change	Total Number of Trials
		Group A (Unrestricted)				
All dilutions	Local	42	3	5*	6	56
	Vein	4	23	8	8	43
	Carotid	3	19	12	0	34
1:10,000	Local	17	2	1	2	22
	Vein	1	8	2	1	12
	Carotid	3	5	10	0	18
1:100,000	Local	24	1	4	4	33
	Vein	3	13	5	7	28
	Carotid	0	14	2	0	16
1:500,000	Local	1	0	0	0	1
	Vein	0	2	1	0	3
	Carotid	0	0	0	0	0
		Group B (Restricted)				
All dilutions	Local	28	3	4*	2	37
	Vein	2	14	5	5	26
	Carotid	1	12	10	0	23
1:10,000	Local	12	2	1	0	15
	Vein	0	4	2	0	6
	Carotid	1	2	8	0	11
1:100,000	Local	15	1	3	2	21
	Vein	2	9	2	5	18
	Carotid	0	10	2	0	12
1:500,000	Local	1	0	0	0	1
	Vein	0	1	1	0	2
	Carotid	0	0	0	0	0

* In three of these cases the artery constricted first and then dilated.

Group A: All experiments except those described in Group C.

Group B:[8] Experiments remaining after the following had been discarded from group A: those in which the blood pressure was below 76

6. Epinephrine tablets (Parke Davis & Co) were dissolved in Ringer's solution (1 cc. of a 1 : 10,000 dilution equals 0.1 mg. of epinephrine).

7. Dial-Ciba with ethyl carbamate was furnished by the Ciba Company, New York.

8. After the local application of epinephrine, the percentage of constrictions as related to the total number of cases in group A was almost identical with that in group B: 75 and 75.7, respectively, and the percentage of dilatation in the two groups was similar: 5.4 and 8.1. After intravascular injection, also, the correspondence between groups A and B was fairly close. The results in group B, however, seem the more reliable, so this group has been used for further study.

mm. of mercury before injection; those in which the results might have been affected by previous experimental procedures, and those in which the control period seemed inadequate. We consider that group B contains the best controlled and most typical reactions to epinephrine.

TABLE 4.—*Effect of the Dilution of Epinephrine on the Average Amount of Change in the Diameter of the Pial Arteries*

Type of Injection	Dilution of Epinephrine 1:10,000	1:100,000	All Dilutions
Local:			
Constrictions (percentage of total trials)	80	71	76
Average constriction (percentage decrease in diameter)	22	16	18
Intravenous:			
Dilatations (percentage of total trials)	67	50	54
Average dilatation (percentage increase in diameter)	11	8	9
Intracarotid:			
Dilatations (percentage of total trials)	18	83	52
Average dilatation (percentage increase in diameter)	28	10	12
Dilatation followed by constriction (percentage of total trials)	73	17	43
Average dilatation (percentage increase in diameter)	13	5	11
Average constriction (percentage decrease in diameter)	8	6	8

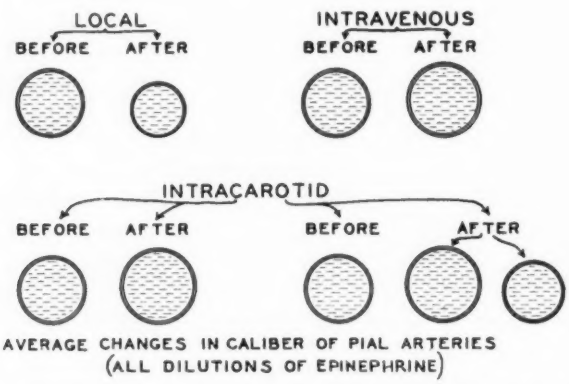

Chart 1.—The circles are drawn to show the average change in the cross-sectional area of the pial arteries after the application of epinephrine by different routes. (As in table 4 the predominant change only is shown.) The average is calculated from the combined results obtained with all three dilutions: the average constriction after local application is 18 per cent; the average dilatation after intravenous injection, 9 per cent; the average dilatation after intracarotid injection, 12 per cent; the average dilatation followed by constriction after intracarotid injection, 11 and 8 per cent, respectively.

Group C:[9] Experiments in which the blood pressure showed no characteristic rise after intravenous or intracarotid injections of epinephrine.

9. Group C is not tabulated, but will be discussed later.

The figures in table 3 clearly show the predominance of constrictions over dilatations when epinephrine was applied locally. After intravascular injection, the predominance of dilatations over constrictions is equally clear.

Another of the interesting relationships shown in this table is the increase in the number of constrictions following dilatations after the intracarotid injection of the stronger solution of epinephrine. In spite of the greater rise in blood pressure, the ratio of simple dilatations to

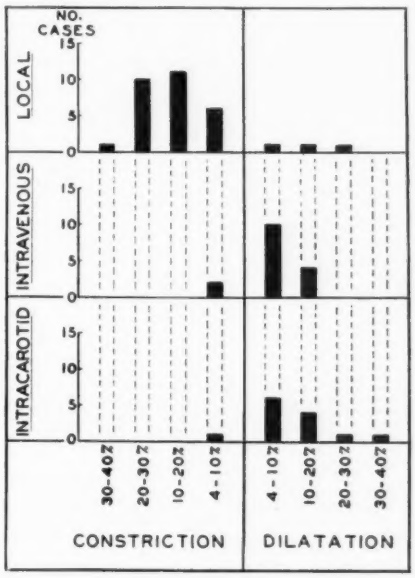

Chart 2.—Those cases in which constriction alone and those in which dilatation alone occurred are divided into groups according to the extent of change (figured in terms of percentage of the initial diameter). The height of each column represents the number of cases in the group designated.

dilatations followed by constrictions was 2:8, whereas with the weaker solution the ratio was completely reversed, i. e., 10:2. The most reasonable explanation of this difference is that when the stronger solution was used, the greater concentration of epinephrine in contact with the walls of the pial arteries caused constriction after the height of the blood pressure reaction was passed.

The effect of the dilution of epinephrine on the average amount of change in the diameter of the pial arteries is given in table 4. Only the predominant change is considered, and the percentage of cases so reacting is recorded.

The extent of the changes in diameter of the pial arteries after the administration of epinephrine by different routes is seen in chart 2. A more detailed analysis of our results is given in table 5.

TABLE 5.—*A. Local Application of Epinephrine* *

Experiment	Diameter of Pial Artery, Microns		Pressure of Femoral Artery Mm. Hg	Cerebrospinal Fluid Pressure, Mm. Ringer's Solution	
	Before Injection	Percentage Change		Before Injection	After Injection
		1:10,000 Dilution			
1.....	180	−25	100	69	..
2†.....	216	−38	...	76	63
3.....	270	−30	...	53	92
4.....	207	−26	108	154	..
5†.....	198	+ 9	82	58	82
6.....	144	−12	110	68	65
7.....	144	+12	84	82	120
8.....	180	− 5	84	69	160
9.....	171	−26	...	109	70
10.....	171	−21	146	98	117
11.....	162	−22	146	98	200
12†‡.....	90	−5 +20	88	142	150
13†‡.....	135	−10	84	107	114
14†‡.....	126	−11	...	119	122
15†.....	217.5	−21	...	155	180
		1:100,000 Dilution			
16.....	171	−5 +5	76	78	60
17.....	225	− 4	...	29	36
18†.....	153	−18	106	30	51
19†.....	234	−17	...	88	200
20†.....	189	−5 +5	86	40	67
21†.....	198	− 2	82	50	67
22†.....	216	−19	...	54	88
23†.....	243	−15	...	58	94
24†.....	207	−22	...	48	57
25.....	117	+23	114	63	69
26.....	144	0	76	65	98
27.....	171	−21	...	88	...
28.....	162	+6 −11	146	105	190
29.....	171	−16	148	120	200
30.....	162	−11	144	90	170
31.....	162	−11	152	115	200
32†‡.....	90	−20	88	132	146
33†.....	234	−19	...	85	90
34†.....	243	−22	...	83	89
35†‡.....	144	− 9	84	120	117
36†‡.....	126	− 7	84	113	119
		1:500,000 Dilution			
37†.....	234	− 6	...	93	94

* One or 2 cc. of the solution was used in irrigating under the cranial window.
† Dial-Ciba was used as the anesthetic. (Amytal was used in all cases not marked.)
‡ Monkey.

In Group C, in more than half the cases the pial arteries under observation showed no change, and in the rest the change was slight, usually being a dilatation, as in groups A and B. It is noteworthy that the dilatation took place when no rise in blood pressure (greater than 12 mm. of mercury) was recorded for the femoral artery.

TABLE 5.—*B. Intravenous Injection of Epinephrine*

Experiment	Dose, Mg. per Kg.	Diameter of Pial Artery, Microns		Pressure of Femoral Artery, Mm. Hg			Cerebrospinal Fluid Pressure, Mm. Ringer's Solution	
		Before Injection	Percentage Change	Before Injection	After Injection	Percentage Change	Before Injection	After Injection
38	0.029	196	+18	88	176 80	+100 −9	29	55 26
39†	0.018	172.5	+13 −9	90	190 80	+111 −11	57	90
40	0.018	243	+11 −11	..	...	.....	39	90
41†	0.015	112.5	+7	80	170	+112	132	180
42	0.014	81	+11	114	160 104	+40 −9	112	129 98
43†	0.013	99	+5	86	164 80	+91 −7	63	84
44†	0.0037	216	+4	76	90	+18	32	13
45†	0.0037	207	+6 −4	78	110	+41	12	4
46	0.0035	144	+12	96	138	+44	72	90 68
47	0.0035	99	+9	104	126 98	+21 −6	87	92 75
48	0.0032	234	+4	120	138 114	+15 −5	112	121 94
49	0.0031	180	−5	112	152 96	+36 −17	43	47 23
50	0.0031	207	+15	82	120	+46	39	47 30
51	0.0031	234	+6	84	120	+43	35	42 27
52†	0.0030	180	0	114	130 104	+14 −9	27	33 18
53†	0.0030	180	−5	112	132 104	+18 −7	26	35 18
54	0.0030	270	+6	114	134	+18	15	22 2
55	0.0030	108	0	110	136 88	+24 −20	33	36 21
56	0.0030	126	+7	96	134 90	+40 −6	54	58 40
57	0.0029	99	+9	82	170	+107	69	84 63
58	0.0028	49.5	+9	100	144 94	+44 −6	59	78
59	0.0028	180	+10 −5	86	144 74	+67 −14	72	87
60	0.0023	180	+3	112	140 104	+25 −7	74	86 57
61	0.0023	216	0	116	170	+47	81	86 76
62†	0.00075	180	+5 −7	92	140	+52	102	111
63	0.00061	216	+6	88	104	+18	37	33

† Dial-Ciba was used as the anesthetic. (Amytal was used in all cases not marked.)

TABLE 5.—*C. Intracarotid Injection of Epinephrine*

Experiment	Dose, Mg. per Kg.	Diameter of Pial Artery, Microns		Pressure of Femoral Artery, Mm. Hg			Cerebrospinal Fluid Pressure, Mm. Ringer's Solution	
		Before Injection	Percentage Change	Before Injection	After Injection	Percentage Change	Before Injection	After Injection
64	0.022	252	−5	102	128 96	+25 −6	52	20
65	0.022	252	+14 −7	88	148	+68	43	79 27
66	0.020	144	+6 −12	94	204 88	+117 −6	73	87 53
67†	0.018	97.5	+27 −12	82	188 78	+129 −5	97	134 93
68†§	0.017	97.5	+38	90	216 64	+140 −29	43	85
69	0.016	108	+17	114	206 94	+81 −18	67	80 64
70†§	0.015	112.5	+7 −7	76	160	+110	116	160
71†§	0.015	112.5	+7 −7	82	160	+95	125	170
72†	0.015	112.5	+13 −7	92	180 70	+96 −24	127	155 120
73†	0.015	105	+7 −7	86	208 60	+142 −30	138	140
74†	0.015	97.5	+23 −8	84	224 70	+167 −17	130	...
75	0.0045	180	+10	76	102 70	+34 −8	59	28
76	0.0040	144	+9	84	100 66	+19 −21	70	58
77†	0.0037	198	+9 −2	88	106 82	+20 −7	9	13 2
78†	0.0036	105	+14	88	118	+34	97	...
79†	0.0036	97.5	+23	84	112 80	+33 −5	92	86
80	0.0030	360	+5 −2	110	130 98	+18 −11	13	0
81†	0.0029	216	+4	80	114	+42	42	47
82	0.0028	207	+4 −6	86	144	+67	88	104
83	0.0023	162	+11	108	126	+17	58	66 45
84	0.0020	144	+19	96	200	+108	78	145 64
85†	0.0015	171	+5 −5	84	136 76	+62 −10	37	30
86	0.0008	171	+5	108	134 96	+24 −11	65	49

† Dial-Ciba was used as the anesthetic. (Amytal was used in all cases not marked.)
§ The left carotid artery was tied off proximal to point of injection.

In some cases there was a fall of from 18 to 24 mm. of mercury, and yet the pial artery dilated slightly. This may have been due to slowing of the blood flow and asphyxial response by the pial artery from retained carbon dioxide (as shown by Wolff and Lennox [10]). In the other cases in which the femoral blood pressure showed no change, it is possible that a rise in arterial pressure did occur in the head. Other evidences of the action of epinephrine were present: dilated pupils, apnea, slow pulse and increased pulsation of the artery.

In addition to this study of caliber change in pial arteries from 50 to 300 microns in diameter, we have examined also the smaller arterioles from 10 to 50 microns in diameter; the fine arterioles of capillary or near capillary size; the fine venules and the larger veins. Judging by simple microscopic observation the fine arterioles, after local application of epinephrine, appear to change little if at all; certainly they never constrict to a point approaching obliteration, and the velocity of blood

TABLE 6.—*Effect of the Local Application of Epinephrine on Pial Vessels, Determined by Photomicrographs*

	Arteries (50-300 Microns)	Arterioles (10-50 Microns)	Arterioles (Less Than 10 Microns)	Veins	Venules
Number times pial vessel constricted.....	23	9	3	23	29
Number times pial vessel dilated.....	4	7	9	2	0
Number times pial vessel did not change..	5	15	17	4	3
Number of trials.....	32	31	29	29	32

flow seems to be not much affected. A more careful study of arterioles and venules by photomicrographs, before and after local application of epinephrine, gives more detailed results, which are shown in table 6.

Analysis of this table shows that of the finest arterioles 59 per cent show no change, 31 per cent show dilatation and 10 per cent show constriction. In the same photographs the larger arteries show a definite constriction in 72 per cent of the cases. Arterioles of from 10 to 50 microns occupy an intermediate position, 29 per cent showing constriction. The veins and venules, on the other hand, show a higher percentage of constrictions than even the larger arteries, i.e. 85 per cent of all cases. The extent of venous constriction, also, is greater.

COMMENT

Several sources of error have been investigated and so far as possible controlled. One cause of the occasional lack of response of the pial arteries to epinephrine or other solutions when used in irrigation beneath

10. Wolff, H. G., and Lennox, W. G.: Cerebral Circulation: XII. The Effect on Pial Vessels of Variations in the Oxygen and Carbon Dioxide Content of the Blood, Arch. Neurol. & Psychiat. **23**:1097 (June) 1930.

the cranial window may be the comparative impermeability of the outer layer of the arachnoid. This is clearly seen if a solution of methylene blue (methylthionine chloride, U. S. P.) is instilled beneath the window and presently washed out again. The cells on the surface of the arachnoid are stained, but the blood vessels beneath this membrane are not stained unless, through injury, there is some tear in the latter. It is possible that with our technic, small tears in the arachnoid usually were made during removal of the circle of dura, so that solutions were able to seep into the subarachnoid space. Twice, when irrigation with epinephrine beneath the window failed to effect a change in the caliber of the pial arteries, the window was removed, and a few drops of epinephrine solution were injected beneath the arachnoid. In both cases the arteries constricted.

The epinephrine solution may diffuse at varying rates through the uninjured arachnoid. If this is true, there should be a difference in reactivity between young and old animals, for the arachnoid of the latter is much thicker. But our observations show no consistent difference in reaction for animals of different ages.

The sudden change in the intracranial pressure due to the removal of corks from the rim of the window to permit replacement of cerebrospinal fluid by epinephine or other solutions may cause slight changes in the pial vessels. We have lessened the importance of this factor by reducing the caliber of the outlet in the rim of the window and by gradually replacing the fluid, which slowly drops out. Also, as a control, we have frequently allowed Ringer's solution to pass beneath the window in the same manner [10a] as the epinephrine and with the same volume of solution warmed to approximately the same temperature. These control irrigations were carried out sixteen times; the artery showed no change eleven times, a brief dilatation three times and a brief constriction twice.

During intracarotid injection, sometimes pulling on the carotid causes a transient dilatation of the pial artery. (Possibly this is due to stimulation of the carotid sinus mechanism, for neither electrical nor mechanical stimulation of the common carotid trunk causes any change in the pial vessels.) Suddenly obstructing the flow in one carotid artery may cause a short constriction followed by dilatation. Any of these factors might have affected slightly our results during intracarotid injections, but after each in turn had been controlled the results showed no significant change. Accompanying the rise in blood pressure caused by epinephrine there is often a short period of apnea and through carbon

10a. In the earlier experiments, the fluid was injected slowly by syringe. Recently both Ringer's and epinephrine solutions have flowed in by gravity from two containers at the same level connected with a common stopcock and heating device, thus insuring more accurate control of temperatures and pressures.

dioxide retention this may cause dilatation. The state of relaxation of the pial artery at the time of the experiment is of great importance, and perhaps this is one of the chief sources of error (or at least of irregularities) in our results. If the vessel is already dilated to an extreme degree, it will show no further dilatation and may prove to be wholly nonreactive. If, on the other hand, it is moderately dilated, it may dilate further, or may constrict even more readily than if it were not somewhat dilated at the start.

In spite of differences in classification, in the dosage of epinephrine and in anesthesia, two points of similarity between our findings and those of Riser stand out clearly. Both of us have found that intravenous and intracarotid injections of epinephrine cause dilatation in most cases, seldom constriction, and that local application almost never causes dilatation, usually constriction (75 per cent of our cases). Franke and Seager's findings are in complete accord with these results. Ley [10b] finds that epinephrine following a previous injection of sodium hydrate causes intense constriction of the pial arteries, but we have been unable to confirm this observation.[10c]

The dilatation of the pial arteries usually seen after intravenous injection of epinephrine occurs during the sudden rise in blood pressure and is evidently caused by it, for when this rise is prevented (as Finesinger and Putnam have shown [11]) constriction results, together with a diminished flow of blood through the head.

It is possible that the dilatation associated with the rise in blood pressure is not merely a passive distention of the arterial walls, but is an active dilatation due to a reflex from the carotid sinus. This point has not yet been settled.

Gibbs and Lennox [12] have recorded a pronounced increase in blood flow in the internal jugular vein in man when a strong dose of epinephrine is injected intravenously, causing a great rise in blood pressure. It seems probable, therefore, that under stress of emotion a suddenly

10b. Ley, J.: Recherches experimentales sur la circulation cérébrale et ses troubles, N. V. Harlem, Holland, Erven F. Bohn, 1932.

10c. Jacques Ley has reported greatly increased constriction of pial arteries with local application of epinephrine after intravenous injection of sodium hydrate and after local application of alkali. He used rabbits with widely opened skull and no window. In cats with a closed skull, we have tried intravenous injection of sodium hydrate before local epinephrine, and we have varied the bicarbonate and salt content of the solution in which the epinephrine is dissolved, but we find no consistent difference in vascular response. The degree of constriction with local epinephrine is approximately the same, even when distilled water is used as a solvent.

11. Finesinger, J. E., and Putnam, T. J.: Cerebral Circulation: XXIII. Induced Variations in Volume Flow Through the Brain Perfused at Constant Pressure, Arch. Neurol. & Psychiat. **30**:775 (Oct.) 1933.

12. Gibbs, F. A., and Lennox, W. G.: Personal communication to the authors.

increased output of epinephrine from the suprarenal gland into the blood stream will result in a transient increase in the volume flow through the brain.

CONCLUSIONS

Epinephrine injected intravenously into anesthetized animals usually causes dilatation of the blood vessels in the pia-arachnoid. This dilatation appears to be a secondary effect caused by the sudden rise in blood pressure induced by the epinephrine. Dilatation follows intracarotid injection also, but in this case the dilatation may give way to constriction when the blood pressure falls.

When applied locally to the surface of the brain, epinephrine causes constriction of the pial arteries. The constriction is never intense. (In our animals it averaged 18 per cent.) It may be overcome by suddenly raising the blood pressure. The small veins and venules above capillary size constrict even more than the arteries, judging from photomicrographs. The finest arterioles usually show no change.

These findings are in accord with the classic conception of Cannon, Bayliss and others that an important function of epinephrine is to increase the blood flow through the central nervous system.

B. ACTION OF PITUITARY AND PITRESSIN ON PIAL VESSELS

In 1928, Wolff published a short paper from this laboratory on the effect of the extract from the posterior lobe of the pituitary gland on the pial vessels. Seven experiments were reported. Constriction seemed to predominate over dilatation (though the results showed both effects), and Wolff concluded that constriction was the characteristic response. The series was too small, however, to warrant generalization, and we decided to obtain more data on the action of this hormone.

EXPERIMENTAL OBSERVATIONS

Using the method of investigation employed by Wolff, we have completed a series of forty-three experiments[13] on twenty-one cats anesthetized with amytal and with dial. In twenty-nine experiments betahypophamine (pitressin) was used; in the rest, pituitary. These two extracts acted in a similar manner, the percentage of total dilatations in relation to constrictions being 77 with pitressin and 79 with pituitary.

13. Fourteen other experiments were discarded for the following reasons: lack of a suitable control period of observations; low blood pressure (less than 70 mm. of mercury), and failure of the blood pressure to show any rise after intravenous injection of pituitary or pitressin. Of these, five showed dilatation, five no change, two constriction and two dilatation followed by constriction.

Our results are summarized in table 7.

TABLE 7.—*Effect of Pitressin and Pituitary on Pial Arteries*

Type of Injection	Trials in Which Pial Arteries Showed				Total Number of Trials
	Constrictions	Dilatations	Dilatations Followed by Constrictions	No Change	
Local	3	11	0	3	17
Intravenous	5	17	2	2	26

Local application was followed either by dilatation alone or by constriction alone in 82 per cent of the cases. Of these, 79 per cent showed dilatation (65 per cent of the total trials). The extent of the average dilatation was 16 per cent.

Intravenous injection was followed either by dilatation alone or by constriction alone in 85 per cent of the cases. Of these, 77 per cent gave dilatation (65 per cent of the total trials). The extent of the average dilatation in this group was 6 per cent. In two instances in which the injection resulted in a double change—dilatation followed by constriction—the blood pressure showed a coincident rise and fall, but the constriction occurred while the pressure was still well above its previous level. After intravenous injection of pitressin, an increased rate of flow was seen in the pial veins. The veins lost their purple tint and became scarlet like the arteries. The effect of pitressin on the caliber of the vessels lasted longer than that of epinephrine.

Further details of these experiments are given in table 8.

SUMMARY

Pituitary and pitressin caused dilatation of the pial arteries in anesthetized animals in 65 per cent of all cases (including both local and intravenous injections) and constriction in 19 per cent. The effect was more prolonged than that of epinephrine. The rate of blood flow through the pial veins was increased, and vessels of all sizes became dilated. The dilatation closely accompanied the rise in blood pressure.

Pituitary differed from epinephrine, especially since the former caused dilatation and the latter constriction, when the solutions were applied locally to the surface of the brain, and no rise in blood pressure was involved.

C. VASOMOTOR RESPONSE IN THE PIA AND IN THE SKIN

In the meninges and brain of higher mammals and of man the existence of vasomotor nerve fibers has long been denied by physiologists. From the teleologic standpoint it would seem that a vasomotor supply to the brain, functioning as elsewhere in the body (i. e., causing constriction when the peripheral vessels constrict), would defeat a

TABLE 8.—*A. Local Application of Pitressin and Pituitary* *

Experiment	Diameter of Pial Artery, Microns: Before Injection	Diameter of Pial Artery, Microns: Percentage Change	Pressure of Femoral Artery Mm. Hg	Cerebrospinal Fluid Pressure, Mm. Ringer's Solution: Before Injection	Cerebrospinal Fluid Pressure, Mm. Ringer's Solution: After Injection
		Pitressin (1:10)			
1	180	+30	92	36	36
2†	126	0	80	..	..
3	189	+14	108	48	57
4	198	+ 9	106	..	..
5	189	0	100	..	..
6†	207	+17	...	27	35
		Pituitary (1:10)			
7	180	+30	92	38	39
8†	117	+ 8	80	..	..
9†	117	+ 8	84	43	83
10	82.5	+18	80	..	..
		Pitressin (1:100)			
11†	162	— 6	84	..	..
12†	126	— 7	80	..	..
13†	207	— 4	..	27	23
14	216	0	..	..	..
		Pituitary (1:100)			
15†	180	+10	..	..	..
16†	126	+ 7	80	..	..
17	120	+19	112	..	..

TABLE 8.—*B. Intravenous Injection of Pitressin and Pituitary* ‡

Experiment	Diameter of Pial Artery, Microns: Before Injection	Diameter of Pial Artery, Microns: Percentage Change	Pressure of Femoral Artery, Mm. Hg: Before Injection	Pressure of Femoral Artery, Mm. Hg: After Injection	Pressure of Femoral Artery, Mm. Hg: Percentage Change	Cerebrospinal Fluid Pressure, Mm. Ringer's Solution: Before Injection	Cerebrospinal Fluid Pressure, Mm. Ringer's Solution: After Injection
			Pitressin (1:10)				
18	207	+4	138	170	+23	159	168
19	90	+15	136	168	+24	98	116
20	198	+7	108	134	+24	156	171
21	99	+5	106	124	+17	67	85
22	99	{+9 —9	86	134	+56	70	90
23	225	+8	128	156	+22	36	58
24	180	+10	86	110	+28	48	60
25	126	+7	72	184	+156	51	66
26	198	+5	80	114	+43	45	54
			Pituitary (1:10)				
27	180	+10	106	188	+77	72	84
28	189	+5	120	140	+17	72	72
29	216	+4	126	140	+11	48	50
30	126	{+3 —7	86	148	+72	46	69
31	126	—7	88	134	+52	42	55
32†	117	+8	86	188	+119	..	..
			Pitressin (1:100)				
33†	189	{+10 —5	108	168	+56	37	43
34†	162	—6	78	100	+28	..	..
35	198	+5	136	146	+7	152	160
36	90	+5	128	138	+8	99	102
37	171	+5	84	94	+12	1	7
38	198	+7	84	96	+14	44	49
39	180	—5	112	136	+21	68	72
40	189	+5	124	146	+18	73	79
41	198	+2	120	142	+18	78	83
42	216	+2	116	142	+22	86	90
			Pituitary (1:100)				
43†	162	—8	82	104	+27	..	..

* One or 2 cc. was used in irrigating under the cranial window. Pitressin (Parke Davis & Co.) was dissolved in Ringer's solution: 1:10 = 1 cc. (20 pressor units) plus 9 cc. of Ringer's solution. Solution of pituitary (Parke Davis & Co. brand) also was dissolved in Ringer's solution: 1:10 = 1 cc. (10 international units) plus 9 cc. of Ringer's solution.

† In these cases a hypertonic solution (from 15 to 30 cc. of 50 per cent urea) had been given previously to lower the intracranial pressure.

‡ The solution (from 0.5 to 1.5 cc.) was injected into the femoral vein.

major function of the circulation: an abundant blood supply to the brain in emergencies.

Nevertheless, within the last few years satisfactory proof has been brought forward that nerve fibers—medullated and nonmedullated—are present on the walls of blood vessels in the pia-arachnoid, the choroid plexus and the brain itself. We refer especially to the histologic findings of Stöhr [14] and of Penfield.[15] Recently, too, strong experimental evidence has been obtained in this laboratory that in cats and monkeys the arteries in the pia are regulated, to some extent at least, by vasomotor nerves.[16] To exactly what extent these nerves control the cerebral blood flow is not yet known. Discussion of the relative importance of this vasomotor apparatus has led, we believe, sometimes to overemphasis, sometimes to underemphasis. In our earlier report all statements of opinion as to the probable importance of this apparatus were avoided. Lack of data prevented an accurate estimate. There is need at present to supply such data in order to evaluate, even roughly, the part played by cerebral vasomotor nerves in the normal control of cerebral blood flow.

Clark [17] and Sandison,[18] studying vessels through transparent chambers inserted in the ears of rabbits, have found the arterioles very rapidly and strongly responsive to a variety of stimuli, far more responsive than the pial arterioles of the cats and monkeys (and a few rabbits) which we have observed. Their animals, however, were not anesthetized. It is interesting that Clark [17] found that the longer the ear chambers remained in place, thereby protecting the vessels, somewhat as the skull protects the pial vessels, the less responsive became the vessels within the chamber. It may be that in his chambers the increasing sluggishness of the arterioles was due to trauma from the artificial environment, but, as Clark suggests, his observation may indicate a general law; namely, that reactivity of arterioles varies inversely with the degree of protection from external physical influences.

In France, Riser [2] and his collaborators found that an intravenous injection of epinephrine sufficient to cause from 70 to 90 per cent constriction of peripheral arteries—subcutaneous, mesenteric and renal—was accompanied by a simultaneous dilatation of arteries in the pia. Never with epinephrine did these investigators see the pial arteries

14. Stöhr, Philipp, Jr.: Mikroskopische Anatomie des vegetativen Nervensystems, Berlin, Julius Springer, 1928.

15. Penfield, Wilder: Intracerebral Vascular Nerves, Arch. Neurol. & Psychiat. **27**:30 (Jan.) 1932.

16. Forbes and Wolff.[1] Cobb, Stanley, and Finesinger, J. E.: Cerebral Circulation: XIX. The Vagal Pathway of the Vasodilator Impulses, Arch. Neurol. & Psychiat. **28**:1243 (Dec.) 1932.

17. Clark, E. R., University of Pennsylvania: Personal communication to the authors.

18. Sandison, J. C.: Anat. Rec. **54**:105 (Sept. 25) 1932.

constrict in intense spasm such as that seen regularly in the peripheral arteries. The authors laid great stress on this point and strongly emphasized the difference in response between the intracranial and the extracranial vessels.

EXPERIMENTAL OBSERVATIONS

We have repeated our previous experiments with epinephrine and those with pituitary (as described in sections A and B of this paper), and finally we have attempted (as Riser has done) to compare in a quantitative way the vasomotor control in the pia with that in the subcutaneous tissue of the ear and in one instance in the mesentery. Our measurements have been made on arteries of approximately the same

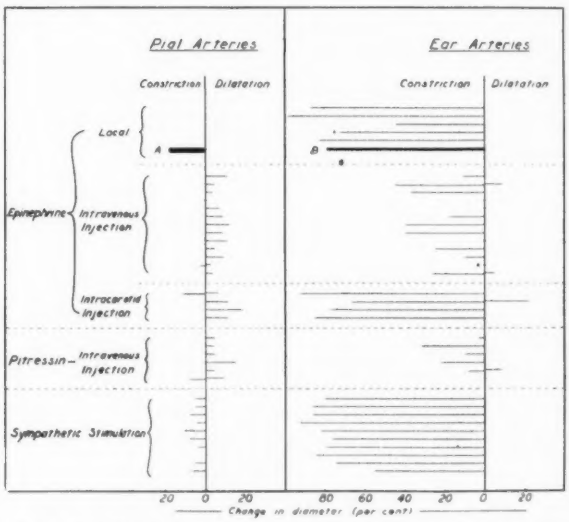

Chart 3.—Each fine line represents a single experiment. The percentage change in the diameter of the pial artery is directly opposite that of the artery in the ear in the same experiment. In the case of the local application of epinephrine, *A* indicates the average constriction in twenty-eight cases. *B* indicates the average constriction of the five arteries the individual constrictions of which are shown. X indicates a mesenteric artery.

size, in the same animal, at the same time, in response to epinephrine, to pitressin and to stimulation of the cervical sympathetic nerve.

The overlying skin of the pinna was removed in these experiments, exposing the underlying tissues, which were kept moist by warm Ringer's solution, frequently applied. The pial vessels were observed through a cranial window as in the previous experiments. Twelve cats and one monkey were studied, and thirty-eight experiments were carried out on these animals.

Measurement of the vessels of the ear was more difficult and less accurate than that of the vessels in the pia. This was due chiefly to the

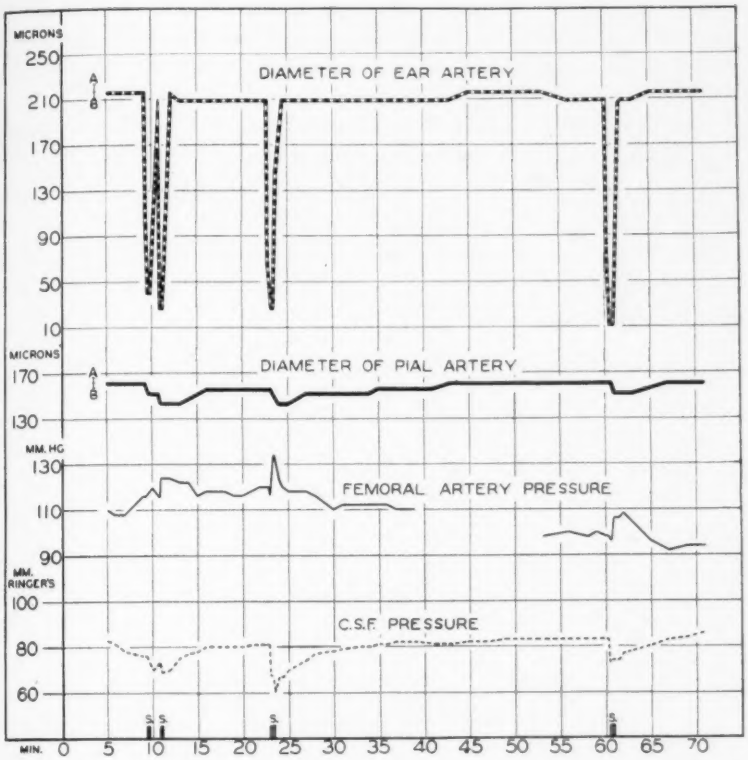

Chart 4.—Sympathetic stimulation in a cat under dial-Ciba anesthesia. The contrast between the reaction of the arteries in the pia and the reaction of those in the ear is shown. The sympathetic nerve was stimulated at intervals as indicated by the cross-hatched areas labeled S along the abscissa. The stimulation was made with faradic current (Harvard inductorium), coil distance 12 cm., applied with bipolar platinum electrodes to the nerve trunk. The four stimulations showed an average constriction of 6 per cent for the pial artery (left parietal region) contrasted with 87 per cent for the artery in the ear. It is worthy of note that the reaction of the artery in the ear is much more rapid throughout than that of the pial artery.

In this and the succeeding charts, ordinates represent the femoral arterial pressure in millimeters of mercury, the diameter of the pial artery and the artery in the ear in microns and the cerebrospinal fluid pressure in millimeters of Ringer's solution; abscissas, time in minutes. (Records were made at intervals of one minute or less.) The broad line, which indicates the diameter of the pial artery, is so plotted that its upper edge records the correct measurements and time relations. The same is true of the broken line, which represents the diameter of the artery in the ear. The short line *A-B* is the extent of the change in the diameter which could be measured accurately. A change of half this extent is of doubtful validity.

irregular surface of the ear and to lack of complete immobilization. Moreover, the surface of the ear was subjected to air currents, change in temperature, drying and other factors, so that spontaneous changes in caliber were more frequent than in the pia. Fortunately, however, the changes in the vessels of the ear were usually so striking that there was no question as to their validity. The results showed a far greater reactivity in the arteries of the subcutaneous tissues of the ear than in those of the pia.

Chart 3 shows the contrast in reaction between the arteries of the pia and those of the ear [19] to epinephrine, to pitressin and to stimulation of the cephalic end of the cut sympathetic nerve.

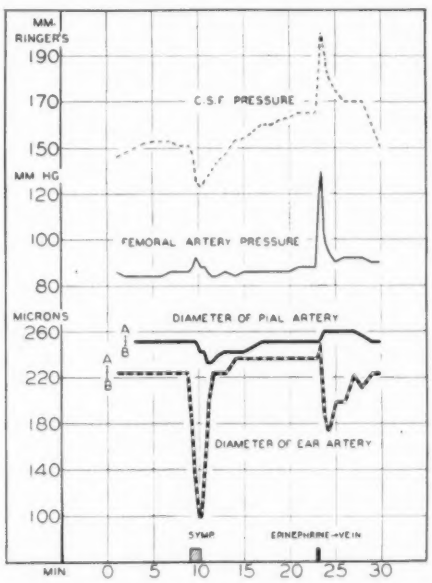

Chart 5.—Sympathetic stimulation and intravenous injection of epinephrine (monkey under dial anesthesia). The cephalic end of the cut sympathetic nerve (on the left) was stimulated. (The coil distance was 12 cm.) The pial artery (left parietal region) constricted 7 per cent, as contrasted with a 56 per cent constriction of the artery in the ear. Twelve minutes later 1 cc. of a 1:100,000 dilution of epinephrine solution was injected into the femoral vein. The pial artery dilated 4 per cent, while the artery in the ear first dilated 5 per cent and then promptly constricted 26 per cent.

After sympathetic stimulation the extent of vasoconstriction in the ear was roughly ten times that in the pia (see chart 3 for group results, and charts 4 and 5 for individual experiments on a cat and a monkey, respectively).

19. This group includes one mesenteric artery, which is indicated on the chart.

After epinephrine had been applied locally to the surface of the ear and of the brain, the extent of vasoconstriction in the ear was about four times that in the pia (chart 3).

After intravenous injection of epinephrine, the artery in the ear usually constricted and the pial artery dilated. The average constriction of the artery in the ear was about 27 per cent, and the average dilatation of the pial artery was 7 per cent (charts 3, 5 and 6).

After intracarotid injection of epinephrine, the artery in the ear usually constricted and the pial artery dilated. The average constriction of the artery in the ear was about 85 per cent, and the average dilatation of the pial artery was 13 per cent (charts 3 and 7).

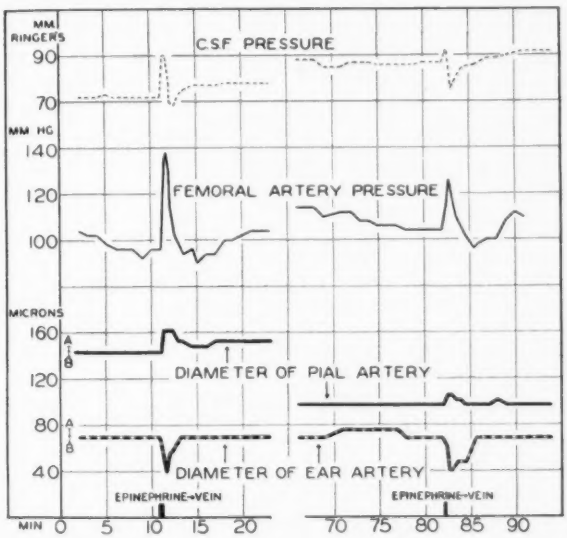

Chart 6.—Two intravenous injections of epinephrine into a cat under amytal anesthesia. The first injection (1 cc. of a 1:100,000 dilution) was immediately followed by a rise in blood pressure of 42 mm. of mercury, a 12 per cent dilatation of the pial artery and a 40 per cent constriction of the artery in the ear. The second injection (1 cc. of a 1:100,000 dilution) caused a rise in blood pressure of 22 mm. of mercury, a 9 per cent dilatation of the pial artery and a 40 per cent constriction of the artery in the ear.

The intravenous injection of pitressin resulted in an average constriction of the artery in the ear of 17 per cent, and an average dilatation of the pial artery of 6 per cent [20] (charts 3 and 8).

The results of these experiments are too variable and the series too small to enable one to place much reliance on the precise ratios given. The figures indicate, however, better than general descriptive terms could do, the relative magnitude of response shown by the subcutaneous arteries compared with the arteries in the pia. The agreement between

20. All these percentages are calculated from the experiments shown in chart 3.

these results and those of Riser and others [2] seems to be close. We agree with Riser, also, that a constriction of the pial arteries established by the local application of epinephrine can be overcome by a sudden rise of blood pressure due to the intravascular injection of epinephrine. In one experiment, epinephrine (0.5 cc. of a 1 : 10,000 solution) was used in irrigating beneath the cranial window. The pial artery constricted 22 per cent. After one minute, epinephrine (0.5 cc. of a

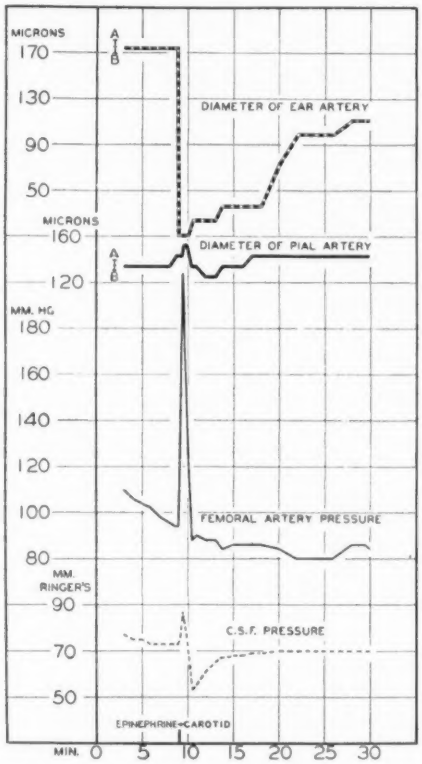

Chart 7.—Intracarotid injection of epinephrine (0.5 cc. of a 1 : 10,000 dilution) into a cat under amytal anesthesia. Traction on the carotid just before the injection caused a 7 per cent dilatation of the pial artery. The injection was immediately followed by a further dilatation of this artery of 6 per cent and then by a constriction of 7 per cent below its original level. This constriction occurred when the blood pressure was falling from its peak. The artery in the ear constricted 93 per cent and was very slow in returning toward its original diameter.

1 : 10,000 solution) was injected into the carotid artery. The femoral blood pressure rose 86 mm. of mercury, and the pial artery dilated 4 per cent with the rising blood pressure and then constricted 15 per cent with the falling blood pressure (31 per cent smaller than the original

diameter). The change in the caliber of the vessel ran closely parallel to the change in the arterial pressure.

In order to test the strength of pial vasoconstriction after nerve stimulation, we tried the following experiment: The cephalic end of the cut sympathetic nerve (on the left) was stimulated by faradic current for three minutes. Thirty seconds after the stimulation started, the pial artery (left parietal region) constricted 8 per cent. Epinephrine (0.5 cc. of a 1:10,000 solution) was then injected into a vein of the leg. The blood pressure rose 44 mm. of mercury, and the pial artery

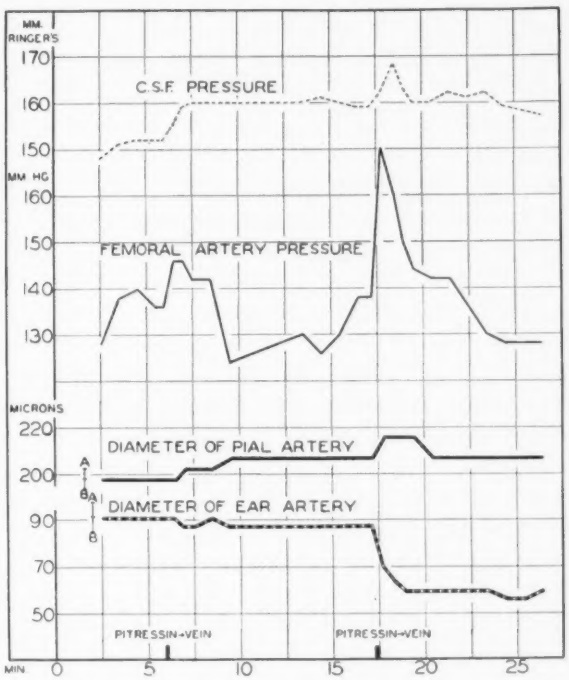

Chart 8.—Intravenous injection of pitressin into a cat under amytal anesthesia. The first injection (1 cc. of a 1:100 dilution) caused a 5 per cent dilatation of the pial artery and a 4 per cent constriction of the artery in the ear. The second injection (1 cc. of a 1:10 dilution) caused a 4 per cent dilatation of the pial artery, which was still dilated from the first injection, and a 32 per cent constriction of the artery in the ear. While the pial artery soon returned to is former diameter, the artery in the ear remained constricted during the period of observation.

dilated 9 per cent while the stimulation of the sympathetic nerve was continuing. The dilatation lasted one and one-half minutes, and then as the blood pressure fell the artery constricted 4 per cent below its initial diameter, and remained thus for two minutes before returning to its original size. It is clear that vasoconstriction due to sympathetic stimulation, like that due to the local application of epinephrine, can be overcome by a sudden rise in blood pressure.

COMMENT

Since these vasomotor constrictions in the pia appear to be feeble when compared with the dilating force of the blood pressure, it might seem reasonable to suppose that under normal conditions the cerebral vasomotor apparatus is of little importance. It should be remembered, however, that these experiments were carried out with anesthetized animals and that the anesthetic probably diminished the vasomotor response. One should take into account, also, the high metabolic rate of the brain. Especially in such active tissue as the cortex, any reduction in blood flow, such as that accompanying even a mild constriction of the cerebral arterioles, is of far greater importance than a similar reduction in a tissue of low metabolism (e. g., the skin). Even though the blood supply to the nerve cells is abundant and the flow more rapid than elsewhere, a sudden reduction in oxygen content or in rate of flow results immediately in symptoms of oxygen lack.

Under pathologic conditions, moreover, it is possible that the vasoconstrictor mechanism may become hyperactive and cause intense spasm of the cerebral arterioles. This possibility has been discussed in a previous paper of this series.[21] Our experimental results give no direct answer to the pathologic problem. We agree with Riser that no intense spasm of the pial vessels in animals under anesthesia can be attributed to vasomotor nerves. The only spasms observed experimentally are those caused by direct mechanical, electrical or strong chemical stimulation of the walls of the vessels.

It may be that the vasomotor apparatus of the brain acts chiefly to keep the cerebral vessels in a proper state of tonus, and especially to regain normal tone after extreme dilatation. This may be the chief function of the cerebral vasomotor nerves, rather than to cause true constriction. Possibly, also, this apparatus may act as a fine adjustment, regulating blood flow within the cranium more precisely than the more powerful hydrostatic or chemical forces.

At any rate, we can say with confidence at the present time that, under the experimental conditions outlined, the magnitude of the vasoconstrictor response within the cranium is far less than that observed in other situations in the body.

SUMMARY AND CONCLUSIONS

The difference between vasomotor activity in the brain (pia) and that in the skin (ear) has been measured in anesthetized animals after epinephrine, pitressin, and sympathetic nerve stimulation.

Pitressin causes dilatation of arteries in the pia; constriction of those in the skin.

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21. Cobb, Stanley: Am. J. M. Sc. **178**:528 (Oct.) 1929.

Epinephrine, by intravenous or intracarotid injection, usually causes a similar response.

Epinephrine, applied locally, causes constriction of arteries in both pia and skin, and the reaction appears to be about four times more intense in the skin than in the pia.

Sympathetic nerve stimulation constricts arteries in both situations—in the skin about ten times as strongly as in the pia.

Vasoconstriction in the pia (of the type described) may be overcome by a rise in blood pressure. In the skin the constriction is not thus overcome.

These results indicate how under stress of strong emotions, as in emergencies, an increase in blood flow through the brain can occur without hindrance from the cerebral vasomotor apparatus.

CEREBRAL CIRCULATION

XXVII. ACTION ON THE PIAL ARTERIES OF THE CONVULSANTS CAFFEINE, ABSINTH, CAMPHOR AND PICROTOXIN

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AND

STANLEY COBB, M.D.

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Twelve years ago, when the experimental study of epilepsy was begun in the Department of Neuropathology of the Harvard Medical School, two main problems were proposed: the clinical study of the biochemical reactions of epileptic patients by Lennox, and the experimental study of convulsions in animals by Cobb. So many leads in the latter problem seemed to point toward vascular changes in the brain, however, and so little was known about the cerebral circulation, that it was decided that the first task was an investigation of the physiology of the cerebral circulation. So far, twenty-three papers on this subject have been published. The present communication is the first to deal directly with experimental convulsions. Since the literature on the cerebral circulation has been recently reviewed in these and other papers,[1] only the work dealing directly with the pharmacologic agents employed in this study will be referred to. In the experiments to be presented, caffeine, absinth, homocamfin, monobromated camphor and picrotoxin were used to produce convulsive seizures in cats. Changes in the diameter of a pial artery were observed directly through a cranial window during the period immediately before the onset of the convulsion, as well as during the seizure. Concomitant changes in the systemic blood pressure and in the cerebrospinal fluid pressure were also recorded.

CAFFEINE CONVULSIONS

A review of previous observations concerning the effect of caffeine on the cerebral vessels was presented in an earlier paper.[2] Intravenous

This work was aided by a grant from the Josiah Macy, Jr., Foundation.

From the Department of Neuropathology, Harvard Medical School, and the Neurological Unit, Boston City Hospital.

1. Cobb, S.: Cerebral Circulation: XXV. Remarks on Clinical Pathology, Ann. Int. Med. **7**:292 (Sept.) 1933. Forbes, H. S.; Finley, K. H., and Nason, G. I.: Cerebral Circulation: XXIV. A. Action of Epinephrine on Pial Vessels; B. Action of Pituitary and Pitressin on Pial Vessels; Vasomotor Response in the Pia and in the Skin, Arch. Neurol. & Psychiat., to be published. Riser, Meriel and Planques: Encéphale **7**:501, 1931.

2. Finesinger, J. E.: Cerebral Circulation: XVIII. Effect of Caffeine on Cerebral Vessels, Arch. Neurol. & Psychiat. **28**:1290 (Dec.) 1932.

injections of caffeine (given as caffeine sodiobenzoate or caffeine chloride) caused dilatation of the pial arteries in cats during amytal anesthesia. In animals which were given caffeine intravenously after ether had been removed, a slight decrease in the diameter of the pial artery under observation was noted immediately after the introduction of the drug. The acute constriction was followed by marked dilatation of the artery. Doses varying from 5.7 to 23.5 mg. per kilogram of body weight were used. A convulsion was never observed with doses of this size. Notkin and Pike [3] were also unable to produce convulsions in cats by using doses of caffeine ranging from $\frac{3}{20}$ to $\frac{11}{20}$ grain (9 to 33 mg.) per pound (0.45 Kg.) of body weight. In other experiments, however, in which doses greater than 23.5 mg. per kilogram were used, marked convulsions, with clonic and tonic movements, were produced, and these are reported here.

Technic.—The technic used in these experiments has been described in detail elsewhere.[4] The animals were given ether anesthesia, and the cranial window was put in place. A manometer recording systemic blood pressure was attached to the femoral artery, and another recording cerebrospinal fluid pressure was connected with the cisterna magna. After these procedures were completed, the ether was removed, in some cases morphine was given, and readings were taken of the diameter of a pial artery, the cerebrospinal fluid pressure and the blood pressure. On the removal of ether, the diameter of the artery decreased, the cerebrospinal fluid pressure decreased and the blood pressure usually increased. When the artery had attained a constant diameter for ten minutes, and the cerebrospinal fluid and blood pressures were reasonably constant for the same period, large doses of caffeine in the form of caffeine sodiobenzoate were introduced intravenously. Constant observations were made by two workers, recording the diameter of the artery the cerebrospinal fluid pressure and the blood pressure. Attention was especially focused on the behavior of the artery before the onset of the convulsion.

Experiments.—Two experiments were made on animals with extremely low blood pressure to see whether the low blood pressure in any way influenced the convulsions. One experiment was made on an animal whose right and left cervical sympathetic nerves were cut, and another experiment, on an animal whose right and left vagi were cut. It was later found that caffeine convulsions could be obtained in animals during amytal anesthesia if only 4 mg. per kilogram (one-half the usual dose) of amytal was given. The results of these experiments are given in table 1. A typical experiment is presented in chart 1.

A male cat, weighing 3.6 Kg., was etherized and prepared for the experiment. The window was put in place; the needle inserted into the cisterna magna was connected with a straight manometer, and the cannula in the left femoral artery was connected with a U-shaped mercury manometer. At this point, the diameter

3. Notkin, J., and Pike, F. H.: Am. J. Psychiat. **10**:771, 1931.

4. Forbes, H. S.: The Cerebral Circulation: I. Observation and Measurement of Pial Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

of the artery was 216 microns, and the cerebrospinal fluid pressure was 62 mm. of Ringer's solution. The ether was removed. During the next twenty-five minutes, the arterial diameter decreased to 198 microns, the cerebrospinal fluid pressure was 35 mm. of Ringer's solution and the blood pressure was 70 mm. of mercury. During the next twelve minutes the diameter of the artery remained constant at 198 microns, the cerebrospinal fluid pressure fluctuated from 31 to 37 mm. of Ringer's solution and the blood pressure was from 70 to 74 mm. of mercury. The final reading for the preliminary period showed the arterial diameter to be 198 microns, the cerebrospinal fluid pressure, 36 mm. of Ringer's solution, and the blood pressure, 72 mm. of mercury. Seven and five-tenths grams of caffeine sodiobenzoate (66 mg. of caffeine per kilogram) was introduced intravenously. Ten seconds

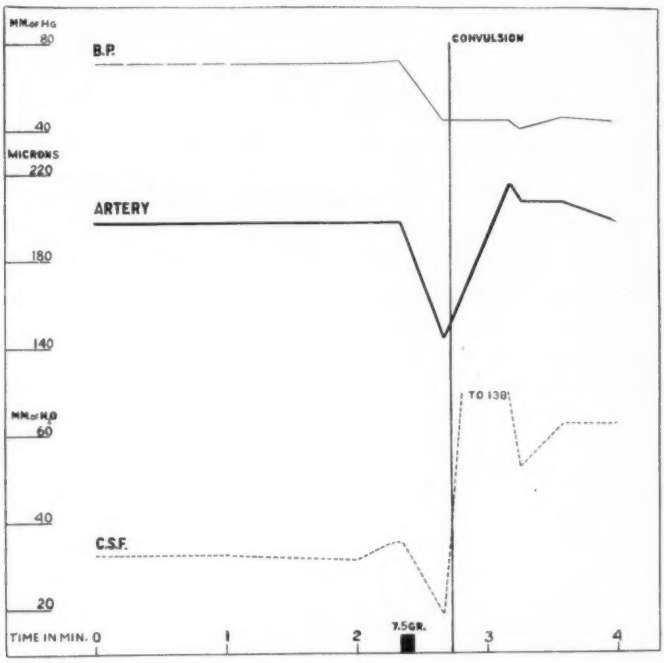

Chart 1.—Caffeine convulsions produced in a cat by the intravenous injection of 7½ grains (0.45 Gm.) of caffeine sodiobenzoate. There is a preliminary constriction in the diameter of the pial artery, accompanied by a drop in systemic blood pressure (*BP*) and in cerebrospinal fluid pressure (*CSF*).

after the caffeine was introduced, the artery began to constrict, and within fifteen seconds the diameter reached 144 microns, a decrease of 27 per cent. The cerebrospinal fluid pressure dropped abrutly from 37 to 19 mm. of Ringer's solution, and the blood pressure, to 44 mm. of mercury. Fifteen seconds after the introduction of caffeine, the artery began to dilate, the cerebrospinal fluid pressure began to rise, and the blood pressure retained its low level. Three seconds after the artery had begun to dilate, the animal had a generalized clonic and tonic convulsion, which lasted about sixty seconds. During the course of the convulsion the artery dilated until its diameter was 216 microns; the cerebrospinal fluid pressure rose

abruptly to 138 mm. of Ringer's solution and then fell to 65 mm., and the blood pressure fluctuated from 46 to 48 mm. of mercury. During the next minute the arterial diameter fell to 207 microns and then rose to 216 microns; the cerebrospinal fluid pressure dropped to 55 mm. and later to 43 mm. of Ringer's solution, and the blood pressure was from 38 to 42 mm. of mercury (chart 1). Before and during the convulsion the animal breathed rapidly and the pupils were extremely dilated.

The data of the experiments on caffeine convulsions are presented in table 1. The results of twenty experiments are tabulated. In all cases caffeine sodiobenzoate was used. In all cases the drug was injected intravenously in large doses ranging from 23.5 to 100 mg. of caffeine per kilogram of body weight. In most cases ether and morphine anesthesia was used as described. In experiments 1, 2, 18 and 21, amytal was used, 4 mg. per kilogram being given intraperitoneally. This is one-half the usual dose given for anesthesia. In this quantity amytal did not inhibit the convulsions caused by caffeine. In experiment 9, chloroform was used as the basal anesthetic, and in experiment 17, ether with bulbocapnine was used. In experiments 2 and 3, the animals were bled to reduce their initial systolic blood pressure in order to determine whether the reaction of the blood vessels was the same in the presence of low blood pressure as with normal systemic blood pressure. Especial attention was paid to changes in the diameter of the artery from the introduction of the drug until the onset of the convulsion. In all experiments there was an acute constriction of the artery following the intravenous injection of caffeine. This preliminary constriction lasted from ten to fifteen seconds. In all cases the animal had a gross convulsion from twelve to nineteen seconds after the artery began to constrict. The onset of the convulsion occurred, however, from two to four seconds after the constriction had begun to relax. In most cases there was marked dilatation of the artery during the seizure, but this was not always true. In some instances the artery returned only to its former size. In other instances the diameter of the artery during and following the convulsive period was less than the diameter during the preceding period. During the actual period of convulsion it was difficult to observe the artery accurately on account of the convulsive movements which shook the microscopic field, but the measurements which we were able to record showed that the dilatation of the artery depended on the severity of the convulsion, with the concomitant changes in respiration, muscle spasm and asphyxia. After the convulsion the artery remained dilated for some time. In most cases a slowing of blood flow was observed in the arteries and in the arterioles during the arterial constriction which took place preceding the convulsion. In no case was a convulsion observed without a preliminary acute vasoconstriction. Arteries ranging from 72 to 324 microns in diameter were observed.

TABLE 1.—*Caffeine Convulsions*

Experiment	Dose		Diameter of Artery, Microns					Blood Pressure, Mm. of Mercury					Cerebrospinal Fluid Pressure, Mm. of Ringer's Solution				
						Per Cent					Per Cent					Per Cent	
	Gm.	Gm. per Kilogram	Basal	Before	After	Before	After	Basal	Before	After	Before	After	Basal	Before	After	Before	After
1	3.5	26	306	209	297	—31	+ 3	30	16	18	—46	—40	17	10	32	— 41	+ 88
2	2.5	23.5	252	144	252	—42	0	12	10	10	—17	—17	17	0	24	—100	+ 41
3	2.5	23.5	252	162	252	—34	0	18	8	14	—55	—22					
4	4	30	72	63	99	—11	+37	150	52	52	—65	—65	46	46	140	0	+204
5	3.5	30	135	72	153	—46	+13										
6	5	39	225	162	216	—28	— 4	120	60	100	—50	—16	80	70	160	— 12.5	+100
7	5	39	180	153	234	—15	+30	122	96	96	—21	—21	38	48	200	+ 26	+420
8	4.5	45	162	153	180	— 5	+11	56	40	64	—30	+21					
9	10	45	189	153	229	—19	+19	86	38	30	—55	—65	12	7	80	— 41	+560
10	4	47	108	90	153	—16	+41										
11	7.5	53	270	144	252	—46	— 6										
12	7.5	58	324	216	324	—33	0										
13	7.5	66	198	144	216	—27	+ 9	92	45	48	—51	—47	56	19	100	— 47	+178
14	7.5	66	207	180	216	—13	+ 4	46	40	40	—13	—13	52	41	90	— 21	+ 73
15	7.5	66	108	63	99	—41	— 8	48	40	34	—16	—29					
16	7.5	66	234	216	298	—13	+35	..	..	..	....	....	56	48	150	— 14	+150
17	7.5	66	108	90	135	— 8	+16	..	..	..	....	....	41	34	72	— 17	+ 75
18	7.5	67	153	126	180	—17	+17										
19	10	74	81	63	108	— 8	+25										
20	15	85	183	108	144	—39	+21	96	50	110	—47	+14	38	5	95	— 87	+150
21	7.5	100	252	153	270	—39	+ 7	..	..	...	....	....	50	10	200	— 80	+300

Although it was impossible to make quantitative observations on arterioles smaller than 9 microns, these smaller vessels were watched, and in all cases a constriction of the arteriole and a slowing of blood flow were seen immediately before the convulsion. During the convulsion, in most cases, the microscopic field became redder, and the smaller vessels became enlarged during the muscular movements and the respiratory changes associated with the convulsion. In two cases observations were made on the behavior of the pial veins; in both cases their reaction paralleled that of the arteries but was quantitatively not so great.

Blood pressure readings were made in twelve of these experiments. In eleven there was a decrease in the blood pressure resulting from the intravenous introduction of caffeine sodiobenzoate. The range of decrease in blood pressure was from 13 to 65 per cent. This decrease, as is shown in chart 1, was usually transitory, the lowest level being reached immediately after the introduction of the drug. In nine experiments the blood pressure remained below the preliminary level. In two experiments it rose slightly above the preliminary level (one of these was experiment 3, which was made on an animal with an initial low blood pressure). These changes in blood pressure are essentially the same as those reported previously [2] when smaller doses of caffeine were given to cats after recovery from ether anesthesia.

Spinal fluid pressure readings were made in twelve of these experiments. In all cases, immediately before the convulsion there was a sudden drop in cerebrospinal fluid pressure, ranging from 14 to 100 per cent. After the convulsion had started, there was a marked rise in cerebrospinal fluid pressure. This marked and abrupt rise was undoubtedly due to the increased intracranial pressure, which in turn resulted from increased venous pressure due to the muscular contractions. The preliminary drop in cerebrospinal fluid pressure was of greater interest. It was at first thought that this drop might have been due to a deep breath taken by the animal just before the onset of the experiment, but the same preliminary decrease in pressure was observed in two animals kept under artificial respiration with the chest open. This emphasizes the fact that the sudden decrease in cerebrospinal fluid pressure is definitely associated with the preliminary decrease in the diameter of the blood vessels. The secondary rise in cerebrospinal fluid pressure during the convulsion is associated with the convulsive movements of the animal, the increased venous pressure and the dilatation of the vessels.

ABSINTH CONVULSIONS

The discovery that absinth could induce convulsions in animals opened many new fields for investigation. The localization of the convulsive focus, the anatomy and physiology of discharging pathways and

the relationship of experimental convulsions to epilepsy are problems which have been approached. Accurate studies have been made on the physiology of the absinth convulsion. Pike [5] and his collaborators determined the minimal convulsive dose and attempted to determine what factors can increase or decrease the dose necessary for the production of an experimental convulsion. Studies have also been made on the circulation of blood in the brain and the meninges. Our concern is entirely with the work on circulation in the brain, and we shall limit the review of the literature accordingly.

Magnan [6] studied fits caused by absinth in patients as well as in animals. In warm-blooded animals (especially dogs), fits could be readily produced by the oral and intravenous administration of absinth. Magnan observed that the vessels of the fundus dilated when the experimental convulsions began. He also noted during a convulsion that the brain was congested and tended to bulge through the trephine opening in the skull. Hill and Nabarro [7] found that after the administration of absinth the cerebral blood flow increased from three to five times. D'Ormea [8] also believed that the intravenous injection of volatile oils caused dilatation of the cerebral vessels. Hill [9] found that the flow from the torcular herophili was increased during convulsions caused by absinth. More recently Cooms and Pike [10] found that there was a preliminary fall in blood pressure after the injection of absinth and monobromate camphor, depending on the size of the dose. There is generally a sharp rise in blood pressure with the onset of the convulsion. During the convulsion the heart rate and the blood pressure are higher. By experiments in curarized animals they showed that this increase in blood pressure is due to the muscular movements. They concluded that absinth is a vasodilator and that there can be no constant vasomotor element in epilepsy.

There is evidence indicating that absinth causes cerebral vasoconstriction either directly or by means of the sympathetic (vasoconstriction) fibers. Uyematsu and Cobb [11] reported that the injection of oil of absinth caused enlargement of the pupils. Later, MacDonald and Cobb [12] reported that shortly before an absinth convulsion in rabbits, they observed blanching of the cortex and a drop in cerebrospinal fluid

5. Pike, F. H., and Elsberg, C. A.: Am. J. Physiol. **72**:337, 1925.

6. Magnan, V.: Recherches sur les centres nerveux, Paris, G. Masson, 1876.

7. Hill, L., and Nabarro, P. N.: J. Physiol. **18**:218, 1895.

8. d'Ormea, A.: Arch. ital. de biol. **40**:141, 1903.

9. Hill, L., in Allbutt: System of Medicine, New York, The Macmillan Company, 1910, vol. 8, p. 1.

10. Coombs, H. C., and Pike, F. H.: Am. J. Physiol. **97**:92, 1931.

11. Uyematsu, S., and Cobb, S.: Preliminary Report on Experimental Convulsions: Convulsions Produced by Administration of Chemical Substances, Arch. Neurol. & Psychiat. **7**:660 (May) 1922.

12. MacDonald, M. E., and Cobb, S.: J. Neurol. & Psychopath. **4**:228, 1923.

pressure. Pike, Elsberg, McCulloch and Rizzolo [13] gave evidence that the autonomic nervous system participates in the general motor phenomena of the convulsive episode. Later Pike and his collaborators [14] saw the blood vessels of the cortex contract just before the onset of the absinth convulsion. These observations were made by looking at the cortex through the open skull, without any attempt at preserving the "closed box" relationship of the skull and its contents. They also noted that there was an increase in the respiratory rate even when the dose of absinth was insufficient to cause a generalized convulsion.

Experiments.—In the experiments to be described an attempt was made to study the effect of varying doses of oil of absinth on the diameter of pial arteries, on the systemic arterial blood pressure and on the cerebrospinal fluid pressure. The technic used was precisely that already described for the study of caffeine convulsions, except that some form of absinth was used. In all cases the drug was administered intravenously to cats which had recovered from light ether anesthesia and which had been given morphine after the ether had been removed.

Two experiments are described in detail.

Small Dose.—A male cat weighing 6.6 Kg. was given ether anesthesia. When the operative procedures had been completed, the diameter of the pial artery measured 144 microns, the blood pressure was 102 mm. of mercury and the cerebrospinal fluid pressure was 80 mm. of Ringer's solution. The ether was removed, and ½ grain (0.03 Gm.) of morphine sulphate was injected subcutaneously. After one-half hour, the arterial diameter reached a level of 126 microns, the blood pressure was 96 mm. of mercury and the cerebrospinal fluid pressure was 40 mm. of Ringer's solution. During a preliminary period of ten minutes, the diameter of the artery remained at 126 microns, the blood pressure at 96 mm. of mercury, and the cerebrospinal fluid pressure at 38 mm. Ringer's solution. After the preliminary period, 0.1 cc. of oil of absinth (0.015 cc. per kilogram of body weight) was injected intravenously. There was an immediate slight drop of blood pressure from 96 to 90 mm. of mercury. Thirty seconds after the administration of the oil of absinthium, the arterial diameter was still 126 microns, the blood pressure was 90 mm. of mercury and the cerebrospinal fluid pressure was 36 mm. of Ringer's solution. Forty-five seconds after the drug had been introduced, there was a slight constriction in the artery, the diameter being 117 microns, a decrease of 7 per cent; the cerebrospinal fluid pressure dropped to 32 mm. of Ringer's solution, and the blood pressure was 88 mm. of mercury. Ten seconds after the artery was constricted, the animal had a mild generalized convulsion which lasted for forty-five seconds, followed by a series of convulsions lasting several minutes. During the convulsions the artery dilated to 126 microns, and it retained this diameter throughout the series of convulsions. The arterial blood pressure dropped to 80 mm. of mercury and then rose to 92 mm. of mercury

13. Pike, F. H.; Elsberg, C. A.; McCulloch, W. S., and Rizzolo, A.: Am. J. Psychiat. **9**:259, 1929.

14. Pike, F. H.; Elsberg, C. A.; McCulloch, W. S., and Chappell, M. N.: The Problem of Localization in Experimentally Produced Convulsions, Arch. Neurol. & Psychiat. **23**:847 (May) 1930.

during the convulsion. The cerebrospinal fluid pressure rose to 110 mm. of Ringer's solution during the first convulsive jerk. It dropped to 35 mm. and then rose to 138 mm. during the following convulsions. After this series of convulsions the experiment was discontinued.

This experiment shows that a small dose of absinth (0.015 cc. per kilogram) brought about a mild convulsion in a cat during light ether and morphine anesthesia. There were a slight constriction of the artery and a slight drop in cerebrospinal fluid pressure and in blood pressure preceding the convulsion. During the convulsion the arterial

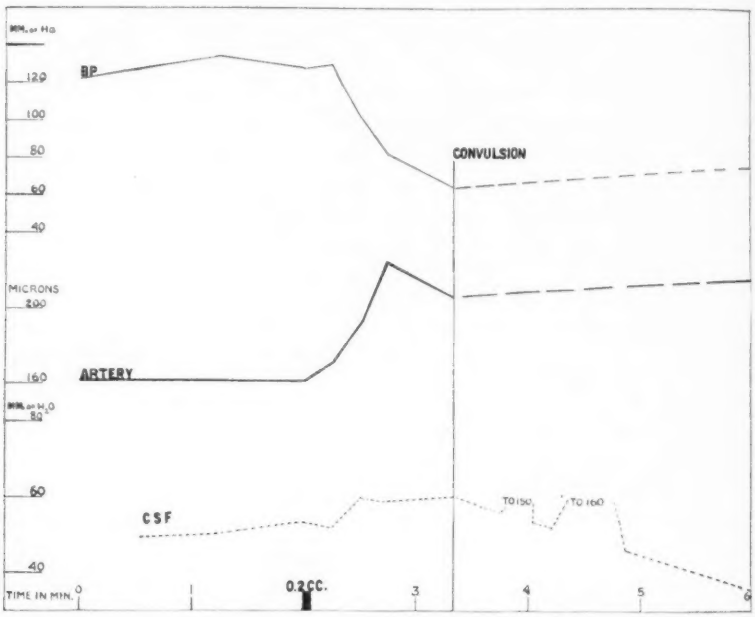

Chart 2.—Absinth convulsion produced in a cat by the intravenous injection of 0.2 cc. of standard solution of oil of absinth. The convulsion was preceded by dilatation of the pial artery, accompanied by a drop in systemic blood pressure (*BP*) and in cerebrospinal fluid pressure (*CSF*).

diameter retained its preliminary level, the cerebrospinal fluid pressure rose considerably and the blood pressure dropped slightly.

Large Dose.—A female cat weighing 4 Kg. was given ether anesthesia. The operative procedures were completed, the ether was removed, and the animal was given ¼ grain (0.015 Gm.) of morphine sulphate subcutaneously. The artery had reached a constant diameter thirty minutes after the ether was removed. During a preliminary period of ten minutes, the arterial diameter remained constant at 162 microns; the blood pressure varied from 124 to 132 mm. of mercury, and the cerebrospinal fluid pressure varied from 48 to 54 mm. of Ringer's solution. At the close of the preliminary period of ten minutes, the animal was given 0.2 cc. of oil of absinth intravenously (chart 2). The artery immediately began to dilate and within forty-five seconds had reached a diameter of 234 microns, an increase

of 44 per cent. It then constricted slightly for thirty seconds, reaching a diameter of 198 microns, when the animal had a convulsion. Immediately after the injection of the oil of absinth, the blood pressure slowly dropped from 124 mm. of mercury, reaching 76 mm. at the onset of the convulsion, a decrease of 38 per cent. The cerebrospinal fluid pressure dropped from 42 to 48 mm. of Ringer's solution; it then rose to 62 mm., where it remained practically constant until the onset of the convulsion. During the series of convulsions, which lasted for two minutes, the artery dilated slightly, from 198 to 207 microns. The blood pressure fluctuated from 76 to 82, always remaining at a low level. The cerebrospinal fluid pressure rose to 150 mm. of Ringer's solution during the height of a convulsion; it dropped to 56 mm. and then rose to 160 mm. during the height of another convulsion. When the animal became quiet, the pressure dropped to 40 mm. After the convulsion had subsided, the experiment was discontinued.

This experiment shows the effect of a larger dose of absinth on the diameter of a pial artery, the arterial blood pressure and the cerebrospinal fluid pressure. The arterial diameter increased considerably and then dropped slightly before the onset of the convulsion. There was a continual drop in blood pressure, and a slight rise in cerebrospinal fluid pressure was noted before the onset of the convulsion.

The results of the experiments with absinth are presented in table 2. Oil of absinth [15] was injected intravenously in all cases, except that in experiments 1, 2, 3, 4, 5, 13 and 14 the standard solution of absinth described by Elsberg and Stookey [16] was used. Doses varying from 0.002 to 0.15 cc. per kilogram were used. In experiment 1 no convulsion was produced, the dosage being too small. Several smaller doses were also used without producing convulsions, and these experiments are not reported. Ether and a combination of ether and morphine were used for anesthesia, as was described in the discussion of the technic. Artificial respiration was used in experiments 6, 7, 20 and 22. Artificial respiration with the chest open was used in experiments 8 and 18. In the other experiments the animals breathed spontaneously.

Our primary interest was focused on the changes taking place before the onset of the convulsions: in the pial diameter, the blood pressure and the cerebrospinal fluid pressure. Great care was taken in noting and recording the data from the time that the drug was administered until the onset of the convulsion. One observer constantly noted the arterial diameter, announcing readings every five or ten seconds. Another observer followed the blood pressure and the spinal fluid pressure readings. A careful attempt was made to obtain all readings synchronously. Observations after the onset of the convulsion were not so accurate; the convulsive movements of the animal jarred the micro-

15. The preparation employed was "Oil Wormwood, American," manufactured by McKesson & Dobbins, Bridgeport, Conn.

16. Elsberg, C. A., and Stookey, B. P.: Studies in Epilepsy: Convulsions Experimentally Produced in Animals Compared with Convulsive States in Man, Arch. Neurol. & Psychiat. **9**:613 (May) 1923.

TABLE 2.—*Absinth Convulsions*

Experiment	Dose			Diameter of Artery, Microns					Blood Pressure, Mm. of Mercury					Cerebrospinal Fluid Pressure, Mm. of Ringer's Solution				
							Per Cent					Per Cent					Per Cent	
	Cc.	Cc. per Kilogram		Basal	Before	After	Before	After	Basal	Before	After	Before	After	Basal	Before	After	Before	After
1	0.4	0.002		162	153	171	— 6	∓ 6	66	60	56	— 9	—15	25	19	30	— 24	+ 20
2	0.8	0.004		81	72	81	—11	0	82	40	54	—51	—34	55	40	37	+ 27	+ 33
3	0.115	0.005		117	108	117	— 8	0	68	46	48	—34	—30	43	57	60	+ 32	+ 40
4	0.015	0.005		135	126	135	— 7	0	66	36	40	—45	—39	51	48	44	— 6	— 14
5	0.02	0.006		198	189	252	— 5	+27	108	103	185	— 5	+71					
6	0.15	0.006		209	180	216	—14	+ 3	...	...	...	....	....	71	65	100	— 8	+ 40
7	0.1	0.015		126	117	126	— 7	0	96	90	84	— 6	—12	38	32	110	— 16	+189
8	0.1	0.03		207	198	216	— 4	+ 4	...	...	...	....	....	79	81	86	+ 3	+ 9
9	0.15	0.041	vein	171	234	189	+36	+10	...	...	...	....	....	72	50	140	— 31	+ 94
				171	216	225	+26	+31										
10	0.2	0.044		234	270	288	+15	+23	...	...	...	....	....	40	32	110	— 20	+175
11	0.18	0.045		189	189	171	0	—10	66	30	42	....	....	48	44	40	— 8	+ 18
12	0.2	0.046		162	225	216	+39	+33	126	84	88	—33	—30	39	59	70	+ 51	+ 79
13	0.15	0.05		135	153	135	+13	0	120	56	50	—53	—58	68	52	67	— 24	— 15
14	0.25	0.05		225	234	225	+ 4	0	78	32	68	—59	—13	75	32	140	— 57	+ 86
15	0.2	0.055		135	135	144	0	+ 7	...	...	...	....	....	4	0	18	—100	+350
16	0.25	0.06		297	306	288	+ 3	— 3										
17	0.3	0.062		198	207	243	+ 5	+23	82	64	..	—21	....	25	29	178	+ 16	+610
18	0.4	0.065		108	135	135	+25	+25	100	48	60	—52	—40	78	86	113	+ 10	+ 19
19	0.27	0.08		99	108	108	+ 9	+ 9	86	56	56	—35	—35	85	75	92	+ 12	+ 8
20	0.4	0.13		90	108	144	+20	+60	114	102	84	—11	—26	94	103	130	+ 10	+ 38
21	0.2	0.13		45	63	63	+40	+40	82	40	32	—53	—60	34	46	46	+ 25	0
22	0.4	0.14		198	216	198	+ 9	0	30	30	36	0	+20	28	33	200	+ 17	+614
23	0.4	0.15		144	153	162	+ 6	+ 9	72	64	88	—11	+22	21	4	130	— 33	+430

scope and its stand and made reading the arterial diameter more difficult. In some cases the animal, by its convulsion, displaced the blood pressure cannula and the cistern needle, making impossible a report on the blood pressure and cerebrospinal fluid pressure.

In experiment 1 (in which no convulsion was obtained) the dose of oil of absinth used was 0.002 cc. per kilogram. In this experiment there was a slight decrease in the diameter of the artery following the injection of the drug. There was also a slight preliminary drop in blood pressure and in cerebrospinal fluid pressure. In the next seven experiments tabulated (experiments 2 to 8) doses varying from 0.004 to 0.03 cc. per kilogram of body weight were used. In these experiments there was a decrease in the diameter of the artery preceding the convulsion. This decrease varied from 5 to 14 per cent. In all the other experiments larger doses were used, which varied from 0.041 to 0.15 cc. per kilogram of body weight; in this group (excepting experiments 11 and 15) there was a dilatation of the artery preceding the convulsion. In experiments 11 and 15 there was no change. The increase in diameter ranged from 3 to 40 per cent. In general, doses of oil of absinth up to 0.03 cc. per kilogram were followed by a constriction of the artery preceding a convulsion. Doses greater than 0.03 cc. per kilogram brought about a convulsion preceded by dilatation of the artery, except in experiments 11 and 15, in which a convulsion took place without any preliminary change in the diameter of the artery.

The changes in arterial diameter observed during and after the convulsion are not so consistent. In experiments 2 to 8, in which small doses were given and in which a preliminary constriction was observed, there was no change in the arterial diameter over its preliminary value in four experiments. In these there was a dilatation ranging from 3 to 27 per cent. In fifteen experiments in which larger doses were used dilatation of the artery was observed during the convulsion in ten instances, the increase in diameter ranging from 4 to 60 per cent. In two experiments there was a decrease in diameter, and in three experiments no change was observed.

Changes in blood pressure were observed in seventeen of these experiments. In all but one there was a drop in blood pressure on the intravenous injection of oil of absinth. The decrease ranged from 5 to 59 per cent. In experiment 22 alone no change was recorded. In eleven cases there was a decrease in blood pressure during and after the convulsion as compared with the preliminary value. In most of these experiments the blood pressure during and after the convulsion was above the minimum value, which was observed immediately on the injection of the drug. In three experiments there was an increase in blood pressure during the convulsion. The cerebrospinal fluid pressure was recorded in twenty-one experiments. In twelve of these experiments there was a decrease in cerebrospinal fluid pressure preceding the con-

vulsion. In nine there was an increase ranging from 10 to 51 per cent. In all cases but one there was a marked increase in cerebrospinal fluid pressure during the convulsion. In many cases the fluid went over the top of the manometer. In other cases, in which readings were taken during the period between convulsions, an increase was observed. The preliminary drop in cerebrospinal fluid pressure is difficult to explain precisely. Before the onset of a convulsion the animal might take a deep breath, which could explain the drop. In six experiments artificial respiration was used to rule out this factor. In two of these the chest wall was open. In these experiments the cerebrospinal fluid pressure paralleled the reaction of the artery; i. e., in experiments 6, 7 and 8 the decrease in the diameter of the artery was associated with a decrease in cerebrospinal fluid pressure, and in experiments 17, 20 and 22 the increase in the diameter of the artery was associated with an increase in cerebrospinal fluid pressure preceding the convulsion.

CAMPHOR CONVULSIONS

In this series of experiments camphor was used in two preparations: homocamfin and monobromated camphor. The technic used was that already described. A typical convulsion caused by an intravenous injection of homocamfin is presented in chart 3.

A male cat, weighing 3.4 kilograms, was given ether anesthesia. The operative procedure was completed; the window was put in place; a cannula was inserted into the femoral artery for reading blood pressure, and a needle was introduced into the cisterna magna for reading cerebrospinal fluid pressure. After these procedures were finished, the ether was removed and the animal was given ¼ grain (0.015 Gm.) of morphine sulphate. About one-half hour after the ether was removed, the artery had attained a constant diameter. During the preliminary period of sixteen minutes, the diameter of the artery remained constant at 243 microns; the blood pressure ranged from 106 to 120 mm. of mercury, and the cerebrospinal fluid, from 52 to 48 mm. of Ringer's solution. After this preliminary period, 0.3 cc. of a 10 per cent solution of homocamfin was introduced into the femoral vein. There was an immediate drop in blood pressure from 120 to 82 mm. of mercury, a decrease of 31 per cent. There was also an immediate drop in cerebrospinal fluid pressure from 48 to 36 mm. of Ringer's solution, a decrease of 25 per cent. The artery had a diameter of 243 microns for twenty seconds after the injection; it slowly constricted during the next eight seconds until its diameter was 225 microns. When the artery constricted, the animal had a gross convulsion. Immediately before the onset of the convulsion, the blood pressure was 96 mm. of mercury, and the cerebrospinal fluid pressure was 20 mm. of Ringer's solution. During the convulsion, which lasted forty seconds, the artery dilated until its diameter was 252 microns. The smaller vessels in the pia dilated, and the whole visible field became considerably redder. After the convulsion was over, the artery constricted to its original diameter of 153 microns. During the convulsion the blood pressure rose to 132 mm. of mercury, and after the convulsion it dropped to 64 mm. It then rose to 104 mm. The cerebrospinal fluid pressure rose to 88 mm. of Ringer's solution during the convulsion and slowly returned to a level of 26 mm. after the convulsion. At this point the experiment was discontinued.

The experiments with homocamfin are summarized in table 3, and the experiments with monobromated camphor, in table 4. Homocamfin was used in thirteen experiments in ten cats. In most cases ether was used for anesthesia, but in some cases ether and morphine were used. In experiment 11, ether and alcohol were used. Artificial respiration with the chest open was used in experiments 3, 4, 5, 6 and 11. Intravenous doses were given ranging from 0.016 to 0.25 cc. of a 10 per cent solution per kilogram of body weight. In all of the experiments, convulsions were produced, and there was a decrease in the diameter of the artery immediately before the onset of convulsions. This con-

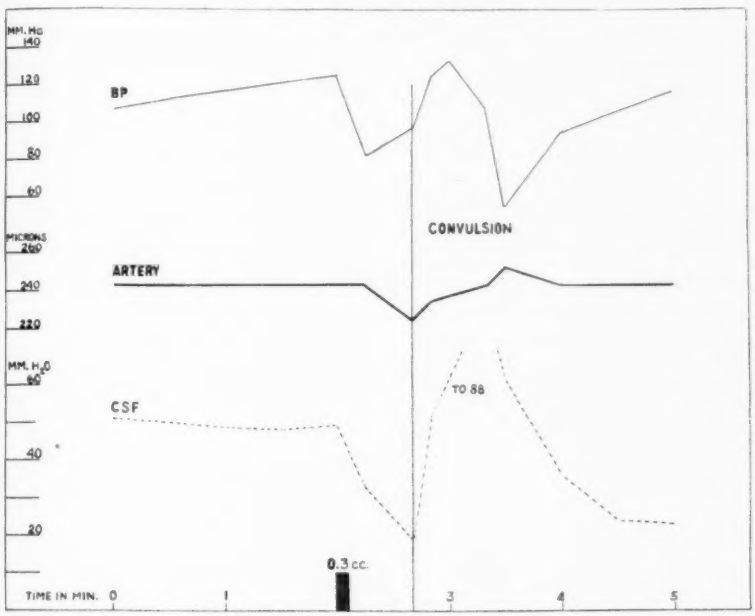

Chart 3.—Homocamfin convulsion produced in a cat following the intravenous injection of 3 cc. of homocamfin. The convulsion was preceded by slight constriction of the pial artery, accompanied by a drop in systemic blood pressure (*BP*) and in cerebrospinal fluid pressure (*CSF*).

striction was not great, the decrease in diameter ranging from 6 to 14 per cent. During the convulsion the artery attained its preliminary diameter in seven experiments. In experiments 1, 8 and 9 it dilated beyond its preliminary level, and in experiments 6 and 10 it remained at its lowest level.

Blood pressure readings were taken in eleven of these experiments. In all cases there was a drop in the systemic blood pressure on the introduction of the homocamfin. In two cases there was an increase in blood pressure during the convulsion, while in nine cases the blood pressure remained below its preliminary level. Cerebrospinal fluid read-

ings were taken in all thirteen experiments. In twelve of these experiments there was a drop in cerebrospinal fluid pressure preceding the convulsion, which varied from 3 to 62 per cent. In experiment 3 there was a slight increase in cerebrospinal fluid pressure before the convulsion. During the convulsion in all cases there was an increase in cerebrospinal fluid pressure which seemed to depend on the severity of the convulsion. In some experiments in which the convulsion was severe the cerebrospinal fluid spurted out over the top of the manometer.

The experiments on the effect of monobromated camphor are presented in table 4. Seven experiments were made on seven cats. In all cases ether-morphine anesthesia was used. Doses of monobromated camphor ranging from 0.06 to 0.18 mg. per kilogram of body weight were introduced intravenously. In experiments 3 and 5 the solutions of "standardized" monobromated camphor described by Wortis [17] were used. In experiments 3, 4, 5 and 6 artificial respiration was used, and in experiments 3 and 6 the wall of the chest was opened. In six cases an increase in arterial diameter was observed preceding the convulsion. The increase was small, ranging from 5 to 22 per cent. In experiment 5 there was no change in the arterial diameter before the onset of the convulsion. During the convulsion an increase in the diameter of the artery over its preliminary value was observed in all cases. The range of increase was from 5 to 43 per cent. The changes in blood pressure following administration of monobromated camphor were not consistent. Immediately after the drug was injected, there was a drop in the systemic blood pressure in experiments 1, 4 and 5. There was an increase in blood pressure in experiments 2, 3, 6 and 7. During the convulsion there was an increase in blood pressure in reference to the preliminary reading in experiments 1, 2 and 6. In experiments 3 and 5 there was a decrease, while in experiment 4 the reading was the same as that during the preliminary period. Preceding the convulsion, there was an increase in cerebrospinal fluid pressure of from 2 to 39 per cent, in six of the seven experiments. In experiment 6 there was a decrease in cerebrospinal fluid pressure. During the convulsion an increase in cerebrospinal fluid pressure was observed in all cases.

PICROTOXIN CONVULSIONS

The technic used was the same as that already described. Picrotoxin was dissolved in distilled water in a concentration such that 1 cc. of solution contained 1 mg. of picrotoxin. The picrotoxin was injected into the femoral vein. Simultaneous measurements of the diameter of a pial artery, the femoral blood pressure and the cerebrospinal fluid pressure were recorded. A typical experiment is presented in chart 4.

17. Wortis, S. B.; Coombs, H. C., and Pike, F. H.: Monobromated Camphor: A Standardized Convulsant, Arch. Neurol. & Psychiat. **26**:156 (July) 1931.

TABLE 3.—*Homocamfin Convulsions*

Experiment	Dose		Diameter of Artery, Microns					Blood Pressure, Mm. of Mercury					Cerebrospinal Fluid Pressure, Mm. of Ringer's Solution				
						Per Cent					Per Cent					Per Cent	
	Cc.	Cc. per Kilogram	Basal	Before	After	Before	After	Basal	Before	After	Before	After	Basal	Before	After	Before	After
1	0.1	0.016	198	180	207	—10	+ 5	82	62	60	—24	—26	34	33	48	— 3	+ 41
2	0.1	0.028	153	144	144	— 6	— 6	46	36	24	—24	—48	94	81	100	—13	+ 49
3	0.2	0.032	180	153	180	—19	0	86	56	66	—35	—25	75	78	100	+ 4	+ 33
4	0.2	0.052	90	85	95	— 6	+ 6	86	84	100	—15	+ 4	52	45	57	—13	+ 9
5	0.2	0.056	180	153	180	—11	0	..	..	...	....	....	59	58	93	— 7	+ 57
6	0.2	0.056	180	171	162	— 5	—10	..	..	...	....	....	58	55	70	— 5	+ 20
7	0.2	0.056	153	135	153	—11	0	52	32	48	—38	— 7	45	20	53	—55	+ 18
8	0.2	0.046	180	171	198	— 5	+10	122	90	108	—26	—11	49	40	130	—18	+ 16
9	0.3	0.088	243	225	252	—14	+ 4	122	84	130	—31	+ 7	48	18	70	—62	+ 45
10	0.3	0.088	252	234	234	— 7	— 7	146	80	120	—45	—17	28	15	54	—46	+ 92
11	0.4	0.105	99	81	99	—18	0	108	62	100	—42	— 7	56	32	53	—43	— 5
12	0.6	0.23	117	108	108	— 8	— 8	82	40	70	—51	—14	68	62	140	— 9	+106
13	0.7	0.25	117	108	126	— 8	+ 7	86	70	50	—18	—41	69	67	110	— 3	+ 59

TABLE 4.—*Monobromate Camphor Convulsions*

Experiment	Dose		Diameter of Artery, Microns					Blood Pressure, Mm. of Mercury					Cerebrospinal Fluid Pressure, Mm. of Ringer's Solution				
						Per Cent					Per Cent					Per Cent	
	Mg.	Mg. per Kilogram	Basal	Before	After	Before	After	Basal	Before	After	Before	After	Basal	Before	After	Before	After
1	0.2	0.06	81	99	116	+22	+43	102	86	120	—15	+17	24	30	68	+25	+183
2	0.2	0.06	198	207	207	+ 5	+ 5	134	144	180	+ 7	+34	66	67	120	+ 2	+ 82
3	0.4	0.08	144	162	162	+12	+12	120	128	110	+ 7	— 8	110	116	250	+ 5	+218
4	0.6	0.15	162	162	180	0	+11	54	38	42	—29	—23	20	26	85	+30	+325
5	0.5	0.15	126	135	144	+ 7	+14	76	28	30	+63	+61	66	55	80	—17	+ 21
6	0.5	0.18	90	108	108	+20	+20	..	..	..	....	....	33	46	90	+39	+172
7	0.2	0.08	189	216	225	+14	+19	126	90	126	—29	0	38	44	94	+16	+121

A cat weighing 2.8 Kg. was given ether anesthesia. The operative procedure was completed, the ether was removed and readings were taken of the diameter of the artery, the femoral blood pressure and the cerebrospinal fluid pressure. During a preliminary period of fifteen minutes, the diameter of the artery remained constant at 180 microns. The blood pressure ranged between 46 and 50 mm. of mercury, and the cerebrospinal fluid pressure was between 56 and 54 mm. of Ringer's solution. After a satisfactory base line had been recorded, 3 mg. of picrotoxin was injected into the femoral vein. Fifteen seconds after the picrotoxin had been injected, the artery constricted from 180 to 171 microns in diameter, the blood pressure rose from 54 to 58 mm. of mercury, and the cerebrospinal fluid pressure rose from 4 to 57 mm. of Ringer's solution. There was also a marked increase in the respiratory rate. Thirty seconds after the introduction of the drug, the arterial diameter was 171 microns, the blood pressure had dropped

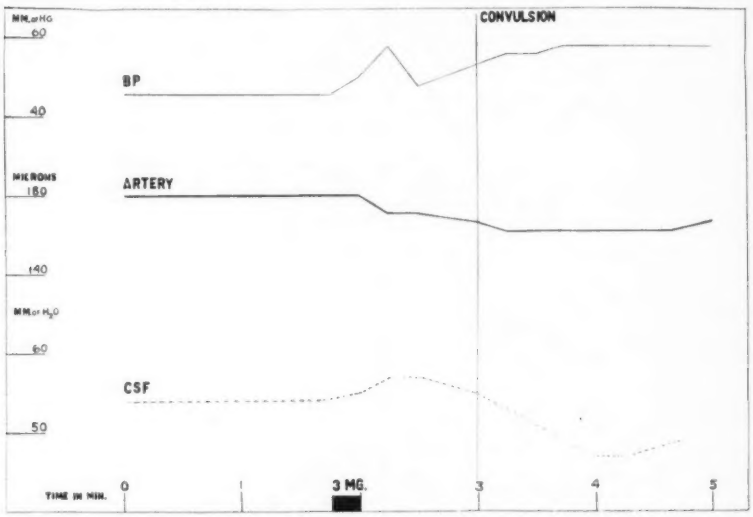

Chart 4.—Picrotoxin convulsion in a cat following the intravenous introduction of 3 mg. of picrotoxin. The convulsion was preceded by slight constriction of the pial artery, accompanied by an increase in systemic blood pressure (*BP*) and in cerebrospinal fluid pressure (*CSF*).

to 48 mm. of mercury, and the cerebrospinal fluid pressure was 57 mm. of Ringer's solution. One minute after the injection, the arterial diameter reached 162 microns, the blood pressure was 56 mm. of mercury and the cerebrospinal fluid pressure was 53 mm. of Ringer's solution. At this point, the animal had a slight convulsion. During the course of the convulsion, when readings were possible, the arterial diameter was 162 microns. The blood pressure rose slightly, but maintained a fairly constant level at 58 mm. of mercury. The cerebrospinal fluid pressure rose during the actual convulsive jerking, but returned to a lower level when the animal quieted down. When the experiment was terminated, the diameter of the artery was 162 microns, the blood pressure was 58 mm. of mercury, and the cerebrospinal fluid pressure was 50 mm. of Ringer's solution.

TABLE 5.—*Picrotoxin Convulsions*

Experiment	Dose		Diameter of Artery, Microns					Blood Pressure, Mm. of Mercury					Cerebrospinal Fluid Pressure, Mm. of Ringer's Solution				
						Per Cent					Per Cent					Per Cent	
	Mg.	Mg. per Kilogram	Basal	Before	After	Before	After	Basal	Before	After	Before	After	Basal	Before	After	Before	After
1	1.3	0.3	72	63	99	−12	+23	100	128	140	+28	+40					
2	2	0.4	162	153	162	− 5	0	68	62	80	− 9	+17	31	8	73	− 70	+135
3	2.5	0.55	126	117	126	− 7	0	130	118	130	− 9	0	72	71	76	− 2	+ 7
4	2.5	0.55	126	117	162	− 7	+28	130	118	130	− 9	0	90	85	140	− 6	+ 55
5	2.4	0.6	225	216	234	− 4	+ 4	96	88	92	− 8	− 4	20	0	40	−100	+100
6	2	0.7	126	126	153	0	+21	110	86	84	−21	−23	91	86	150	− 5	+ 64
7	1.5	0.7	126	117	198	− 7	+45	120	126	110	+ 5	− 8	46	37	95	− 19	+106
8	1.5	0.8	135	117	153	−13	+13	...	...	...	....	....	49	43	90	− 12	+ 74
9	5.2	0.8	270	243	279	−10	+ 5	88	32	...	−63	....	40	35	45	− 12	+ 12
10	5	1.08	180	162	198	−10	+10	46	56	58	+21	+26	59	51	68	− 14	− 15
11	5	1.4	307	298	316	− 3	+ 3	110	108	120	− 2	+ 9	89	81	108	− 10	+ 21
12	3.3	1.9	280	252	298	−14	+14	74	86	56	+16	−24	85	80	90	− 6	+ 6
13	4	2	135	126	135	− 6	0										
14	4.2	2	90	81	126	−10	+40	76	80	64	+ 5	−21	53	40	140	− 14	+164
15	7	7.3	189	180	198	− 5	+ 5	..	..	..	....	....	90	85	120	− 5	+ 33

Fifteen experiments are reported in table 5. These were all done on cats, as already described. Ether-morphine anesthesia was used in ten of these experiments, and ether alone in five. In experiments 4, 5, 11 and 15 artificial respiration was used. In experiments 4 and 15 the chest was opened.

Doses of picrotoxin ranging from 0.3 to 2.3 mg. per kilogram were introduced intravenously. In fourteen of the experiments there was a slight constriction of the artery before the onset of the convulsion, the decrease in diameter ranging from 4 to 14 per cent. In one of the cases in which readings were possible after the onset of the convulsion, there was an increase in the diameter of the artery over the preliminary value. In experiments 2 and 3 the reading was the same as that during the preliminary period. In experiments 8 and 10 there was a slight decrease in diameter as compared to the preliminary period.

The changes in blood pressure were not consistent. Readings were taken in twelve experiments. In seven of these experiments there was a decrease in blood pressure of from 2 to 13 per cent on the injection of the picrotoxin. In five experiments there was an increase in blood pressure. During the convulsive period an increase in blood pressure was noted in four experiments, a decrease in five, and no change in two (as compared with readings during the preliminary period).

The changes in cerebrospinal fluid pressure seemed more consistent. Readings were taken in thirteen cases. In all of these there was a decrease in cerebrospinal fluid pressure preceding the convulsive seizure. This decrease ranged from 2 to 100 per cent. During the convulsion the cerebrospinal fluid pressure rose considerably, depending on the intensity of the convulsion. When the animal became sufficiently quiet for readings to be made, the cerebrospinal fluid pressure was higher than the preliminary level in all cases but one. There was a marked increase in the respiratory rate immediately on the introduction of the drug. This increase always preceded the convulsion, and its probable effect on the variables measured will be discussed later.

COMMENT

The experiments reported were undertaken in an attempt to answer the question: "Do convulsant drugs produce their effects by direct action on the cerebral blood vessels?" A great deal has been written on this problem, especially in regard to absinth, but as far as we can learn no one has directly observed blood vessels by using the cranial window. Our primary concern was with the behavior of the pial arteries immediately before the onset of the convulsion. We also recorded observations on the arterial diameter, the blood pressure and the cerebrospinal fluid pressure during the convulsion.

The intravenous injection of caffeine, homocamfin and picrotoxin produced a constriction of the pial artery under observation immediately preceding the convulsion. The constriction preceding the caffeine convulsion was as a rule considerable, ranging from 5 to 46 per cent. A slowing of the blood flow was also observed in the arteries and in the arterioles. The preliminary constriction produced when homocamfin and picrotoxin were used was not as great, and as a rule not as sudden, as that observed when caffeine was used. Changes in the speed of the blood flow were rarely observed except after caffeine. In the experiments with absinth both preliminary constrictions and preliminary dilatations were seen, depending on the amount of absinth introduced intravenously. Monobromated camphor introduced intravenously caused dilatation.

It is significant that two different camphor compounds appear to cause different changes in the diameter of pial arteries before the onset of a convulsion. The fact that homocamfin gave a preliminary constriction followed by a convulsion, and that monobromated camphor in the doses used gave a preliminary dilatation, indicates that the convulsion was not dependent on the status of the artery. It seems reasonable to postulate that the camphor had a direct action on the nerve tissue and that this action occurred whether the vessel had constricted or dilated before the onset of the convulsion. This point is illustrated even more clearly where absinth convulsions are considered. In most cases small doses caused constriction of the artery followed by a convulsion, whereas large doses produced dilatation followed by a convulsion. Obviously the convulsions followed the use of absinth no matter what the preliminary status of the artery happened to be.

It must be borne in mind that these observations were made on pial arteries in only one small area. Recent work by Finesinger and Putnam [18] indicates that vessels throughout the whole of the pia and the parenchyma of the brain react similarly and together to various stimuli; e. g., when the vasomotor nerves were stimulated, and epinephrine or histamine was injected. This suggests that all the blood vessels of the brain, whether superficial or deep, acted in the same way as the vessels observed in our experiments. However, it is possible that the blood vessels at the base of the brain or within the parenchyma in certain distant areas may have acted otherwise. We know of no data throwing light on this possibility, yet feel that it must be given consideration.

It is of interest to determine precisely how these convulsant drugs caused changes in the cerebral vessels. Previous experiments in this laboratory have emphasized the possibility of several mechanisms being

18. Finesinger, J. E., and Putnam, T. J.: Cerebral Circulation: XXIII. Induced Variations in Volume Flow Through the Brain Perfused at Constant Pressure, Arch. Neurol. & Psychiat. **30**:775 (Oct.) 1933.

at work. In the first place, it is well known that the diameter of pial arteries may change as a result of changes in the systemic blood pressure. This mechanism is best illustrated in the case of the injection of caffeine into animals after ether anesthesia, and has been discussed elsewhere. Recently, Gibbs,[19] using a different technic, observed that caffeine convulsions were preceded by a decrease in blood flow and by a drop in the systemic blood pressure. When he gave epinephrine with the caffeine, the systemic blood pressure did not drop and the convulsion took place without the preliminary slowing in the rate of flow. In our experiments the fact that the preliminary constriction took place even when the cervical sympathetic nerves and the vagi in the neck were cut shows that the vasomotor impulses have little effect on the preliminary constriction caused by caffeine in convulsive doses. The dilatation reported in most cases during and after the convulsion was probably due to the changes in venous pressure, the respiratory changes and the muscular exertion of the convulsion; also one must consider the local action of the caffeine on the wall of the blood vessel.

In the case of every drug used, three factors must be considered: vasomotor changes, the local effect on the wall of the vessel, and changes secondary to variations in systemic pressure. The observed change is probably a sum or equilibrium resulting from these factors. Different preparations and different doses of the same drug will influence these mechanisms in different degrees. When absinth was used intravenously, an immediate drop in the systemic blood pressure occurred in all cases but one. Yet the arterial behavior was not always constant, as one would expect if the secondary effect alone were responsible. Small doses of absinth gave a slight preliminary constriction, whereas large doses gave a preliminary dilatation. This would make us believe that both the vasomotor mechanism and the local muscular mechanism were involved in the reaction. There are some data indicating that absinth stimulates the sympathetic system, and it is possible that small doses tended to cause a constriction by this means. Nevertheless, when large doses were used the respiratory and local changes were great enough to mask the vasomotor changes.

It is even more difficult to understand the behavior of the pial arteries when monobromated camphor and picrotoxin were used. After monobromated camphor there was in most cases a dilatation followed by a convulsion. In three cases there was a drop in blood pressure, and in three a rise in blood pressure. When picrotoxin was used, there was a slight preliminary constriction in all cases. At the same time a drop in blood pressure was observed in seven instances and a rise in five. The question of the changes in blood pressure after picrotoxin was dis-

19. Gibbs, F. A.: Personal communication to the authors.

cussed by Pollock and Holmes.[20] In general our results corroborate theirs and also the results of Coombs and Pike.[10] It is difficult for us to explain the consistent constriction of the pial arteries in the face of marked differences in systemic blood pressure.

Measurements of the cerebrospinal fluid pressure were also taken during these experiments. In general, it may be stated that the spinal fluid pressure reflected the size of the cerebral vessels. In many experiments, just before the onset of a convulsion the animal took a deep inspiration, which was followed by a sudden drop in cerebrospinal fluid pressure. This drop, we believe, was caused by changes in the intrathoracic pressure which affect cerebral venous pressure. Control experiments with artificial respiration and an open thoracic cavity showed that in general there was a preliminary drop in cerebrospinal fluid pressure whenever a preliminary constriction of the pial arteries occurred; likewise there was a preliminary rise in cerebrospinal fluid pressure whenever a preliminary dilatation was observed. During the actual duration of the convulsion there was always a marked increase in cerebrospinal fluid pressure. This was apparently secondary to the changes in venous pressure following the muscular and respiratory changes associated with the convulsive seizure. When the fit was over the cerebrospinal fluid pressure usually returned to its previous level.

In these experiments we have shown that convulsions induced by certain drugs may occur following a preliminary vasoconstriction or a preliminary vasodilatation. No explanation is offered as to how these drugs produce their convulsive effects. Since fits are produced in the presence of both constriction and dilatation, it seems that the state of the blood vessels is not the essential factor. It also seems reasonable to assume that these drugs do not act by producing acute anoxemia, for they do not seem to cause any marked change in the color of the blood, and their vasomotor effects are variable. It is our impression that the drugs act directly on the nerve cells in some way as yet unknown. There are many possibilities, all of which at present are theoretical conjectures.

It is possible that our results may have been influenced by the anesthesia used. After considerable experimentation with various types of anesthesia, we found it most expedient to conduct these experiments as described. Ether was used during the operative procedure; morphine was then injected and ether removed. The drugs were not administered until the pial artery had attained a constant level after ether had been removed and until the superficial reflexes were present. It is probable that all animals were not in the same state of narcosis, even after the superficial reflexes had returned, and it is possible that the variations

20. Pollock, L. J., and Holmes, W. H.: A Study of Respiration and Circulation in Picrotoxin Convulsions, Arch. Int. Med. **16**:213 (Aug.) 1915.

in blood pressure and in arterial diameter in some instances were due to the variations in the state of narcosis. This point has been previously discussed in relation to caffeine.

Studies of this nature are interesting from the pharmacologic point of view. In the present state of knowledge there are so many unknown variables involved in studies of these convulsant drugs that it is difficult to analyze and to interpret the experiments. Each drug seems to have properties all its own and to react in an individual way. Conclusions drawn from the study of one convulsant drug cannot be applied to another, even though the preparations are closely related. It is probable that studies of convulsant drugs have little or no direct bearing on the problems of human epilepsy. Even though the final epileptic discharge as a behavior pattern may have many elements in common with these experimental seizures, the sequence of events may be entirely different. Moreover, in human epilepsy the chain of events leading to convulsive seizures is rarely, if ever, the same in any two cases.

The changes observed in the behavior of the pial vessels are apparently controlled by several mechanisms. In this paper we have been able to give a partial analysis of the mechanisms involved when caffeine and absinth were used. It seems that the behavior of cerebral blood vessels will eventually be understood only by isolating and studying each mechanism independently. It is along such lines that future work should progress.

SUMMARY

1. Caffeine convulsions caused by the intravenous administration of large doses were preceded by an acute constriction of the pial artery under observation, a drop in systemic arterial pressure and a decrease in cerebrospinal fluid pressure.

2. Absinth convulsions following the intravenous introduction of small doses were preceded by slight constriction of the pial artery, a drop in blood pressure and a slight drop or rise in cerebrospinal fluid pressure. Convulsions following large doses of absinth were in most cases preceded by dilatation of the pial artery, a drop in systemic blood pressure and a rise in cerebrospinal fluid pressure.

3. Homocamfin convulsions were preceded by slight constriction of the pial artery, a drop in systemic arterial blood pressure and, as a rule, a decrease in cerebrospinal fluid pressure.

4. Monobromated camphor convulsions were preceded by dilatation of the pial artery and, as a rule, an increase in cerebrospinal fluid pressure. The changes in blood pressure were inconsistent.

5. Picrotoxin convulsions were preceded by slight constriction of the pial artery and a decrease in cerebrospinal fluid pressure. The changes in the blood pressure were not consistent.

CEREBRAL BLOOD FLOW PRECEDING AND ACCOMPANYING EXPERIMENTAL CONVULSIONS

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Recent investigations have done much to strengthen the theory that epileptic convulsions may have a vascular origin. The early observation of Leonard Hill that convulsions can be produced by interfering with the blood supply to the brain has been abundantly confirmed. An accumulation of evidence, brought forward chiefly by Forbes and Wolff [1] and by Cobb,[2] points to the existence of a nervous mechanism which, when stimulated, produces a constriction of the cerebral blood vessels. The question arises as to whether the convulsions produced in animals by certain convulsants frequently used in the experimental study of epilepsy are produced through the mechanism of diminished cerebral blood flow. I have investigated the effect on cerebral blood flow of five commonly employed convulsants.

METHODS

The blood flow recorder used has been previously described.[3] It consists essentially of a needle with an electrically heated tip, the temperature of which is read by means of thermojunctions in series with a galvanometer. The theory on which this instrument operates is exceedingly simple. If a needle supplied with a constant amount of heat is thrust into vascular tissue, the temperature of the needle will vary, other conditions remaining constant, with the flow of blood through the tissue; it will cool off if the flow is increased; it will heat if the flow is decreased.

Under ether anesthesia two small holes were made in the skull of a cat by means of a burr, one through the right and the other through the left parietal bone. The needle was thrust into the left parietal cortex. In order that changes in body temperature should not introduce a serious source of error, the cold junction of the thermojunction circuit was thrust into the right parietal cortex.

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1. Forbes, H. S., and Wolff, H. G.: Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

2. Cobb, S.: The Cerebral Circulation: IX. The Relationship of the Cervical Sympathetic Nerves to Cerebral Blood Supply, Am. J. M. Sc. **178**:528 (Oct.) 1929; Causes of Epilepsy, Arch. Neurol. & Psychiat. **27**:1245 (May) 1932.

3. Gibbs, F. A.: A Thermo-Electric Blood Flow Recorder in the Form of a Needle, Proc. Soc. Exper. Biol. & Med. **31**:49 (Oct.) 1933.

The holes were filled with bone wax, and the animal was allowed to recover from the ether. By passing a constant current through the heating circuit a constant amount of heat was supplied to the needle tip. A running record of the difference in temperature between the needle tip and the unheated cerebral cortex was made by recording graphically the electromotive force in the galvanometer circuit. In order to make sure that the recorder was responding to changes in flow, pressure was applied at intervals over the carotid arteries. A record of the normal blood flow was taken for five minutes. The convulsant was then administered and a record was taken of the flow preceding and accompanying the convulsion. In two instances, in order to establish the responsiveness of the recorder, the animal was reanesthetized and the intracranial pressure was raised while the blood flow and arterial pressure were being recorded (chart 1). In order to make sure that the

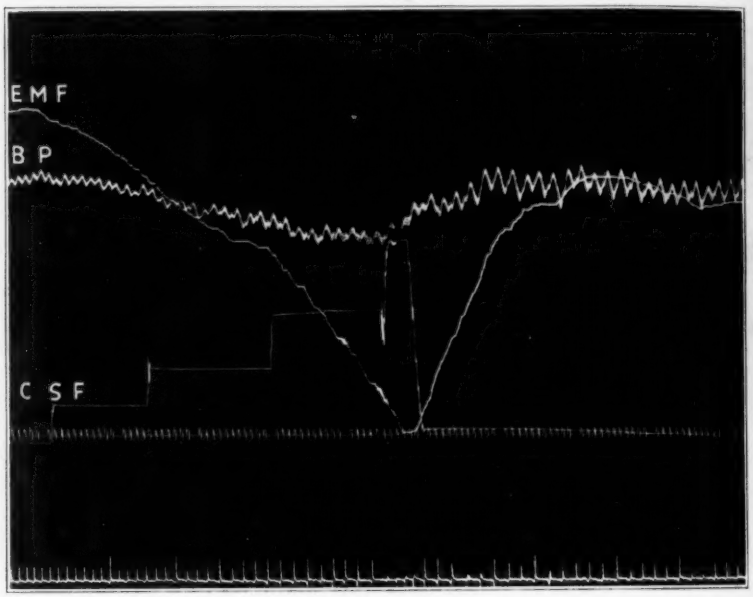

Chart 1.—Record showing the manner in which the blood flow recorder indicated a decrease in the cerebral blood flow (*B P*) when the pressure of the cerebrospinal fluid (*C S F*) was raised. The recorder was inserted in the left parietal lobe, with the cold junction in the right parietal lobe. Because a decrease in flow results in an increase in the temperature of the needle and consequently in an increase in electromotive force, an increase in electromotive force (*E M F*) is recorded as a movement of the writing arm toward the base line. A blood pressure cannula was inserted in the femoral artery, and the record of the pressure was made by means of a mercury U-manometer, with the time record as a base line. The line *C S F* is a record of the pressure (recorded with a mercury U-manometer, with the time record as a base line) in the pressure bottle connected with the cisterna magna through a hollow needle. The time marker records intervals of five seconds and skips a signal each minute. Except where otherwise stated, the methods of representing the recordings are similar in the subsequent charts.

instrument was not responding to changes in body temperature, records were made of convulsions occurring when no heating current was passing through the needle. A typical record of this experiment is shown in chart 2.

EFFECTS OF VARIOUS CONVULSANTS

Oil of Absinthium.—In all of the four cats which received a convulsant dose of oil of absinthium by stomach tube the cerebral blood flow was increased. In no animal did a significant decrease in flow precede the convulsion (chart 3). During the convulsion the flow was greatly

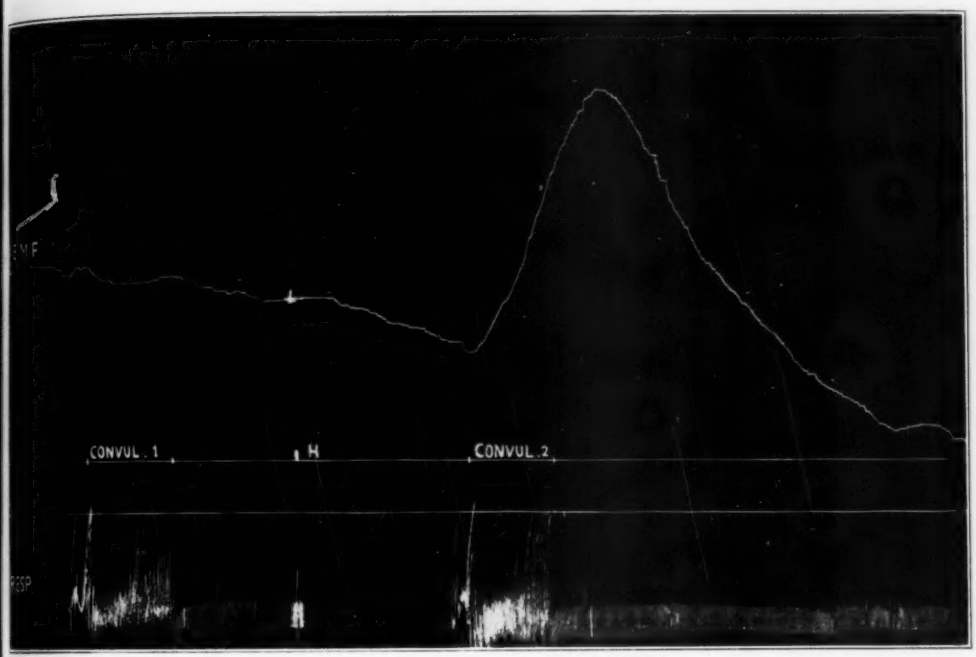

Chart 2.—Record of the electromotive force in the thermojunction circuit during convulsions produced by electrical stimulation of the cortex. At the point marked *H* the heating current was turned on and the recording arm was readjusted. Convulsion 1 was produced while no heating current was being passed through the needle. Convulsion 2 was produced while the heating current was on. It may be seen from the record of the electromotive force during convulsion 1 that no significant difference in temperature between the needle tip and the cold junction occurred; this gives assurance that the variations in the electromotive force in convulsion 2 were not due to changes in body temperature unequally transmitted to the needle tip and to the cold junction.

increased in each animal; following the convulsion it rapidly decreased to a level below that prevailing before the onset of the convulsion.

Camphor.—Convulsant doses of camphorated oil administered by stomach tube tended to increase the cerebral blood flow in the four

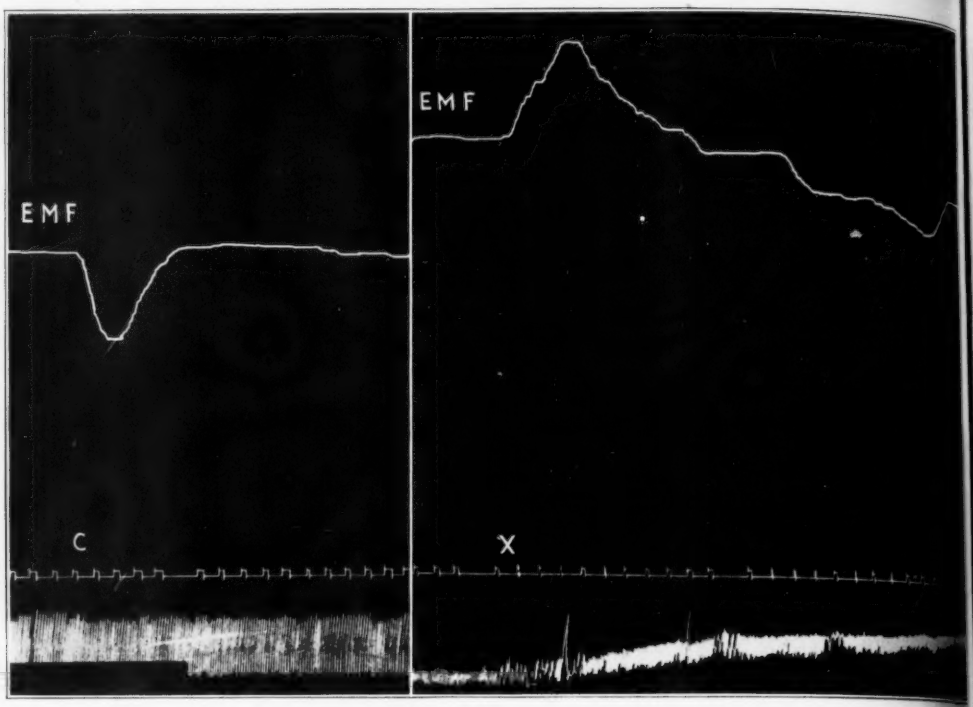

Chart 3.—Blood flow through the left parietal lobe preceding and accompanying the convulsion produced by oil of absinthium. At *C* pressure was applied over the carotid arteries. Oil of absinthium was subsequently administered (3 cc. per kilogram by stomach tube). At *X* a convulsion occurred. The end of the convulsion is indicated by the resumption of regular respiration.

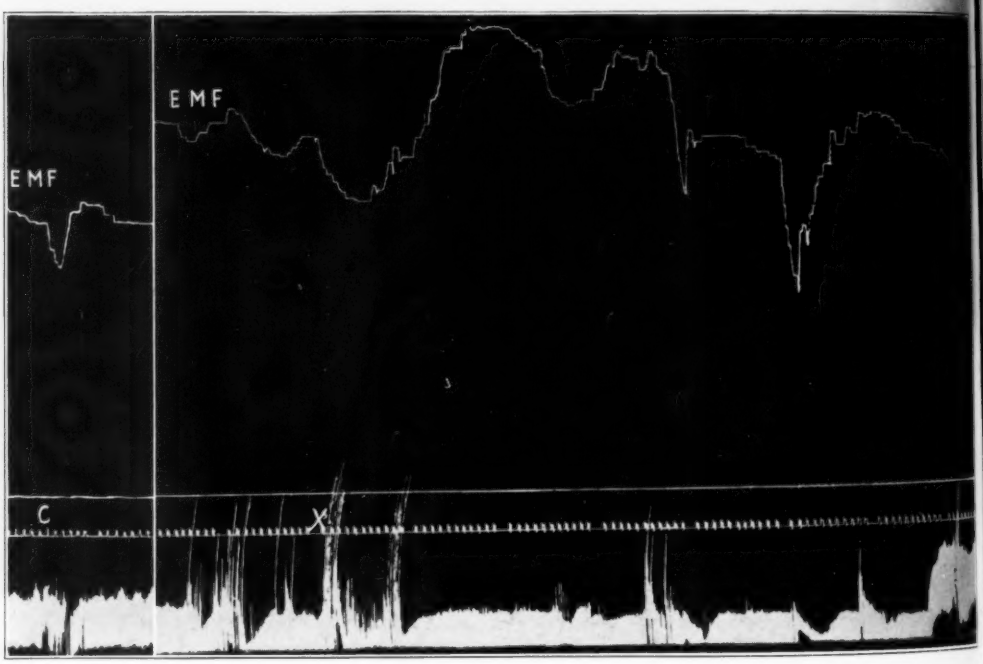

Chart 4.—Blood flow through the left parietal lobe preceding and accompanying the convulsion *X* produced by camphorated oil. At *C* pressure was applied over the carotid arteries. Subsequently camphor was administered (2 Gm. per kilogram by stomach tube).

animals used for the experiment. In each animal the flow showed much variation; it was greatly increased one minute and greatly decreased the next. In two animals the convulsion occurred after a marked decrease in flow; in two experiments the convulsion appeared in the face of an increased cerebral blood flow (chart 4). By pressure on the neck marked reductions in blood flow could be produced which were greater and of longer duration than those occurring as the result

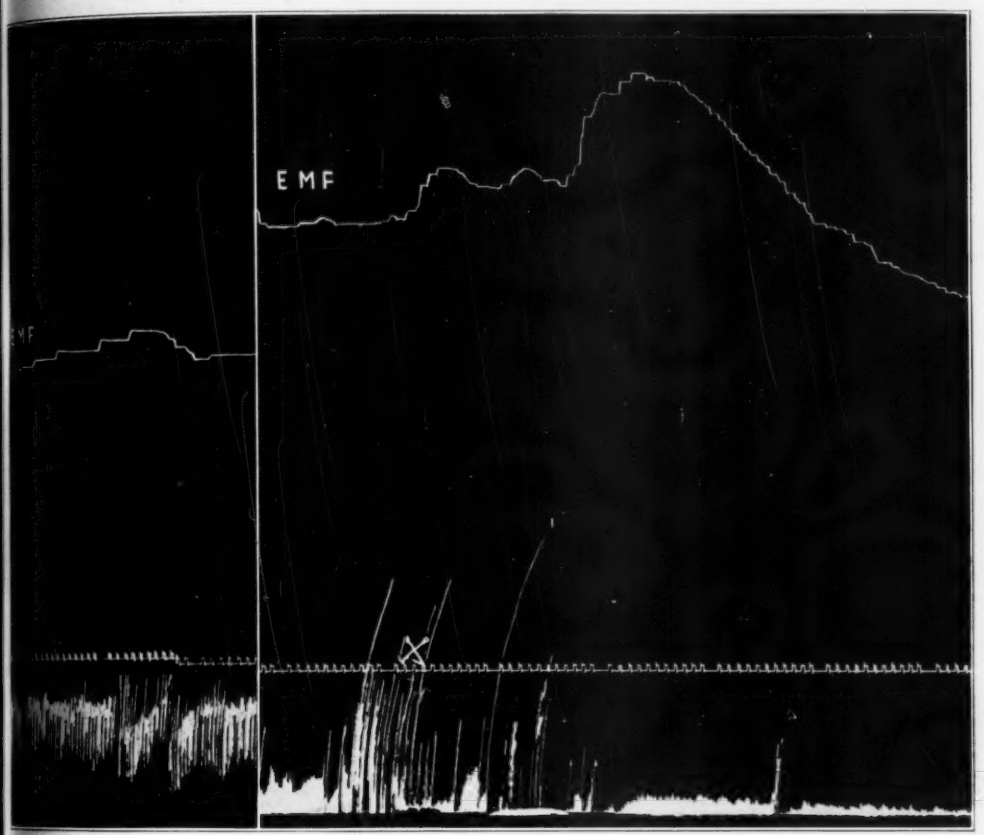

Chart 5.—Blood flow through the left parietal lobe preceding and accompanying the convulsion *X* produced by picrotoxin. The record on the left shows the level of the blood flow preceding the administration of picrotoxin (10 mg. per kilogram subcutaneously).

of the administration of the drug. These were, however, insufficient to produce convulsions. In each animal the cerebral blood flow was conspicuously increased during the convulsion. Following the convulsion it fell either to the level prevailing before the onset of the convulsion (one instance), or below that level (three instances).

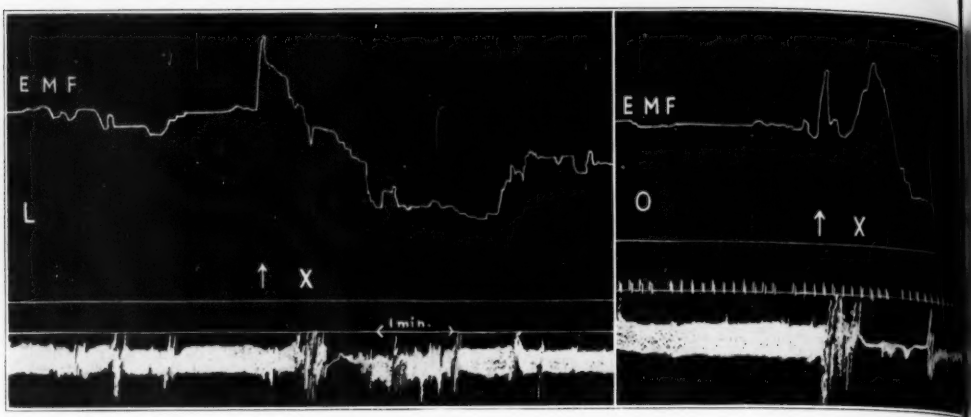

Chart 6.—Blood flow through the left parietal lobe preceding and accompanying the convulsion *X* produced by caffeine. The time scale in record *L* is indicated by "1 minute" enclosed in brackets. The time marker in record *O* is similar to that in figure 1. At the point indicated by the arrow in record *L*, 1 Gm. of caffeine per kilogram was injected intravenously. At the point indicated by the arrow in record *O*, 1 Gm. of caffeine and 1 cc. of a 1 : 10,000 solution of epinephrine hydrochloride per kilogram were injected intravenously. The initial increase in flow occurring at the time of the injection was apparently caused by manipulation of the femoral vessels.

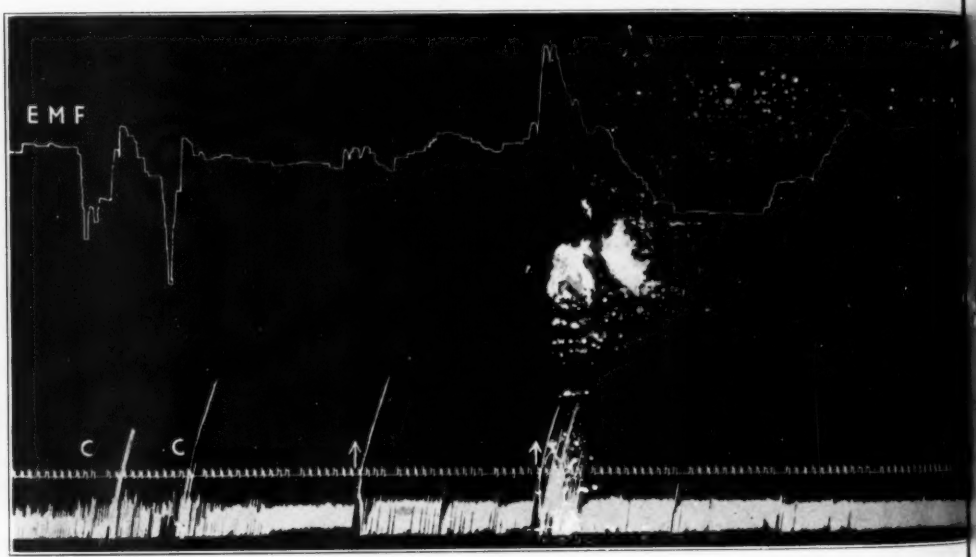

Chart 7.—Blood flow through the left parietal cortex preceding and accompanying the convulsion *X* produced by induction shock applied in the region of the motor cortex. The cortex was stimulated by means of a fine unipolar electrode introduced through a small drilled hole in the skull. At *C* pressure was applied over the carotids. A the point indicated by the first arrow the cortex was stimulated with a current too weak to produce a convulsion. At the point indicated by the second arrow a stronger current was used.

Picrotoxin.—In the three animals subjected to experiments with convulsant doses of picrotoxin the cerebral blood flow was increased. In none of these animals did a decrease in blood flow as great as that produced by light digital pressure on the neck precede the convulsion (chart 5). During the convulsion the flow increased greatly. As the convulsion terminated the flow fell rapidly to a level considerably below that prevailing before the onset.

Caffeine.—Convulsant doses of caffeine administered intravenously decreased the cerebral blood flow in the three animals studied. The convulsion was occasionally preceded by a slight additional decrease in flow. If, however, epinephrine hydrochloride was administered with the caffeine, the amount of caffeine required to produce a convulsion was not increased and the convulsion occurred in spite of a greatly increased flow (chart 6). An increase in flow accompanied the convulsion; at its termination the flow fell rapidly to a level below that prevailing before the convulsion.

Electrical Stimulation.—In four animals induction shocks of sufficient strength to produce a convulsion were applied to the cerebral cortex in the region of the sigmoid gyrus. There was no significant decrease in the cerebral blood flow preceding the convulsion. In each animal as the convulsion developed the flow increased greatly. The flow decreased rapidly, however, when the convulsion ended, falling to a level considerably below that previously prevailing.

COMMENT

The nature of the experiment made it seem desirable to limit the number of animals used to the smallest that would yield definite answer to the question under investigation: Do certain convulsant agents produce convulsions by decreasing the cerebral blood flow? Because of the possibility that a decrease in blood flow might precede a convulsion without being the cause of the convulsion, it was believed that a few negative experiments would outweigh the evidence of many positive ones. Negative experiments were so readily obtained that an accumulation of numbers seemed unwarranted.

Some doubt may arise as to whether the presence of the needle and the application of heat may have abolished vasomotor responses in the vessels near the needle. This is certainly not the case when the needle is placed in the kidney or in the temporal muscle.[3] It seems likely that, even though the vasomotor response of the cerebral vessels is more easily abolished than the vasomotor response of the vessels in other tissues, this response would not be abolished in areas somewhat removed from the needle. Such areas would probably be supplied by arteries or drained by veins lying near the tip of the needle. Changes in flow in the surrounding reactive areas would be mirrored by changes in flow in

the large vessels in the nonreactive area around the needle, and so, though the recorder would not show the marked change in flow that it would if the surrounding arterioles and capillaries were reactive, it would still record a change. The instrument could hardly fail to give evidence of a general vasoconstriction so intense as to compare in its effect on the cerebral blood flow with the ligation of all the large arteries in the brain, the procedure usually employed to produce convulsions in cats by diminishing cerebral blood flow.[4] It may be noted that the instrument was perfectly capable of recording the decrease in the cerebral blood flow which occurred when the animal's neck was gently squeezed, a decrease which was apparently too slight to produce a convulsion.

It is possible, however, that localized vasoconstriction did occur at a distance from the needle, in the hypothalamus for instance, and that this vasoconstriction played a rôle in the production of the convulsion. On this point the present study has no evidence to offer.

CONCLUSIONS

Oil of absinthium, camphorated oil, picrotoxin, caffeine and induction shock do not produce convulsions by causing a general diminution in the cerebral blood flow.

4. Gildea, E., and Cobb, S.: The Effects of Anemia on the Cerebral Cortex of the Cat, Arch. Neurol. & Psychiat. **23**:876 (May) 1930.

VENTRICULOGRAPHIC INTERPRETATION

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Since the time of Dandy's initial description of ventriculography [1] and encephalography [2] there have been many publications of the ventriculographic findings in abnormal cases.[3] But surprisingly little attention has been paid to the true anatomic significance of the gas shadows of the normal ventricle. This oversight has resulted in glaring mistakes in ventriculographic interpretation, published unwittingly. It has resulted further in diagnostic errors (usually unpublished) which were due not to the true limitations of the method but rather to a lack of knowledge of the basic principles of interpretation.

In order to pass judgment on departures from normal, it is best first to analyze normal ventricular shadows. To this end we have prepared a bronze model of the human cerebral ventricles in a partial cast of the skull [4] (fig. 1). This model was constructed by one of us (A. T.) after an analysis of injection casts of the ventricles, a study of over 400 selected cases of ventriculography or encephalography and careful dissection of the brain in a manner which will be described in a subsequent publication by him.

The lateral view of the ventricles has frequently been illustrated and offers few difficulties of interpretation as compared with the antero-posterior and postero-anterior views. We shall therefore consider pri-

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From the Department of Neurology and Neurosurgery of McGill University.

Read at the Fifty-Ninth Annual Meeting of the American Neurological Association, Washington, D. C., May 9, 1933.

1. Dandy, W. E.: Ann. Surg. **68**:569, 1918.

2. Dandy, W. E.: Ann. Surg. **70**:397, 1919.

3. Grant, F. C.: Ventriculography and Encephalography, Arch. Neurol. & Psychiat. **27**:1310 (June) 1932. Foerster, O.: Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:512, 1925. Pancoast, H., and Fay, T.: Am. J. Roentgenol. **21**:421, 1929. Dixon, H., and Ebaugh, F. G.: Encephalography, Arch. Neurol. & Psychiat. **28**:1326 (Dec.) 1932. Jüngling, O., and Peiper, H.: Ventrikulographie und myelographie in der Diagnostik des Zentralnervensystems, Leipzig, Georg Thieme, 1926.

4. Reproductions of this model may be obtained from the Pilling Surgical Instrument Company of Philadelphia.

marily the latter views, but before doing so, we may add a word as to the technic of posturing the head for roentgenography.

Only those parts of the ventricle which are completely filled with gas reveal themselves clearly. It is essential that some one familiar with the

Fig. 1.—Bronze model of ventricles in base of skull.

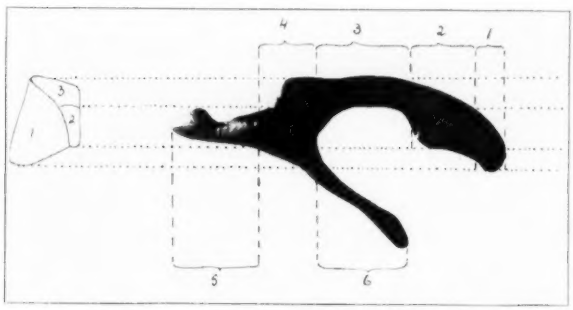

Fig. 2.—The lateral ventricle divided into six portions which are visible as units in anteroposterior views. The dotted horizontal lines serve to project portions *1*, *2* and *3* on an imaginary plate. These lines would be approximately parallel to the base of the skull.

clinical problem should be present in the x-ray room to manipulate the head between exposures so as to cause the gas *to fill completely* those parts of the ventricle which are being studied from a clinical point of view.

ANTEROPOSTERIOR AND POSTERO-ANTERIOR VIEWS OF THE VENTRICLES

It may be seen in figure 2 that the lateral ventricle has been divided into six portions or shadows which, for convenience, are numbered from *1* to *6*. Each of these shadows may be seen in anteroposterior views as distinct units, as will be described. If the anterior portion of the ventricle is seen in an anteroposterior view when the brow is up, the portions *1*, *2* and *3* are represented as in figure 3.

Shadow 1.—This shadow is thrown by the anterior horn as it passes forward laterally and downward. In figure 4 a frontal section has been made through the anterior horn. If air filled the anterior horn only back as far as the level of this brain section, the shape of the shadow would be outlined as indicated in the sketch immediately above the photograph. If air filled the horn to a somewhat more posterior level, the

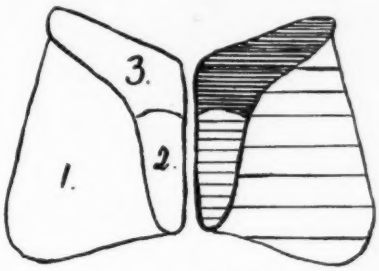

Fig. 3.—Outlines of portions *1*, *2* and *3* in an anteroposterior view.

shadow would increase by enlargement mesially and upward. To express it in another way, the less air there is in the anterior horn, the smaller the shadow is and the farther lateral and downward. If the x-ray plate is placed beneath the occiput instead of above the brow, the anterior horn is, of course, magnified falsely.

It is obvious that many observers have been misled into believing that the darker outline formed by shadows *2* and *3* represented the anterior horn. This mistake has been rendered the easier by the fact that in the development of the plate the technician, in his effort to intensify shadows *2* and *3* which first attract his attention, may allow the faint outline of shadow *1* to disappear. If the plates are taken on the following day, it often happens that the air which formerly filled *2* and *3* has been absorbed, leaving only enough to fill portion *1*. Then the x-ray technician, in his effort to demonstrate air, stops the development of the plate at such a point as to show this shadow clearly. As a result the shape of the ventricle seems to the unwary clinician to have changed, whereas in reality the appearance of change is due only to a comparison between *2* and *3* as seen on the first day and *1* as seen on the second.

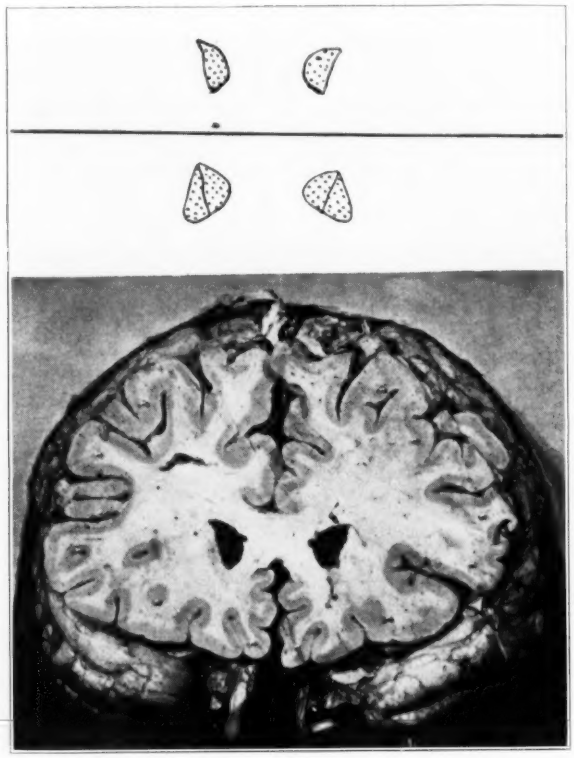

Fig. 4.—Frontal section of the brain through the anterior horn.

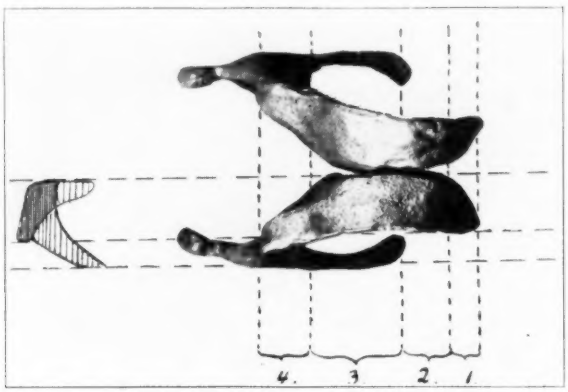

Fig. 5.—The ventricular model seen from above.

Shadow 2 (fig. 2).—Shadow *2* represents that portion of the lateral ventricle which is situated in front of the thalamus and posterior to portion *1*. It is overlapped to some extent by shadow *1* and is bounded laterally by a sharp line formed by the inner surface of the caudate nucleus. It is bounded mesially by the septum pellucidum. Above, it overlaps shadow *3*. If there is no filling of portion *3*, the complete shadow of portion *2* has the outline seen in figure 6.

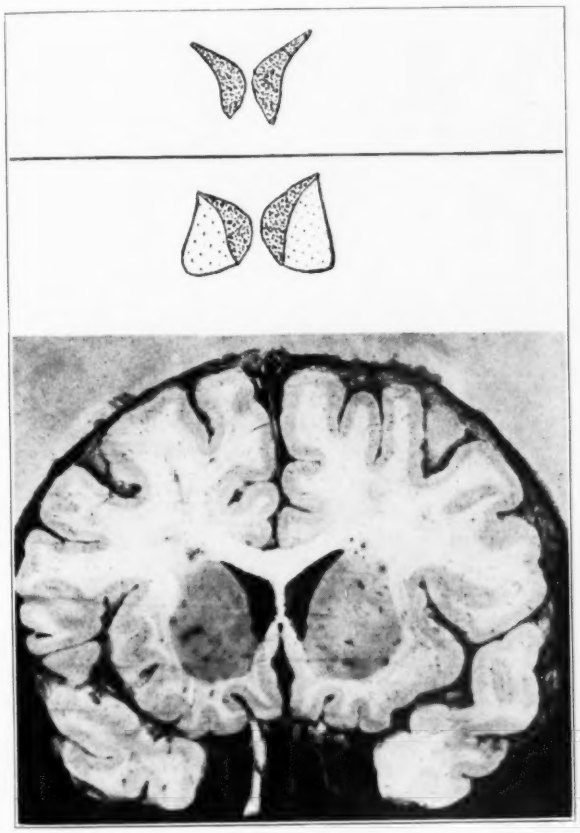

Fig. 6.—Frontal section of the brain through portion *2*.

Portion *1* deviates from the midline and therefore cannot be responsible for shadow *2*, and the latter is too low to be confused with portion *3* (fig. 2). Portion *4* of the ventricle, as shown in figure 5, lies too far laterally to come into consideration here.

In case the head is tipped backward when the plate is taken, so that the anterior portion of the ventricle is situated at a higher level than the thalamus, shadow *2* does not appear as a separate entity but is merged into one outline with shadow *3*. In figure 6 a frontal cross-

section of the brain has been made through portion *2*. If air fills the ventricles only back to the level of this section, the combined picture of *1* and *2* will be that seen in the sketch immediately above the photograph (fig. 6). In such a case, *2* is represented by an evenly dark shadow without the superposition of *3* as in figure 5.

Reference to the projections of the ventricular shadow on the x-ray plate seen in figure 7 *A, B, C,* illustrates the fact that shadow *2* gradually merges with *3* as the head is tipped backward. This figure also illustrates the fact that shadow *1*, the anterior horn, becomes shorter and shorter as the head is tipped backward.

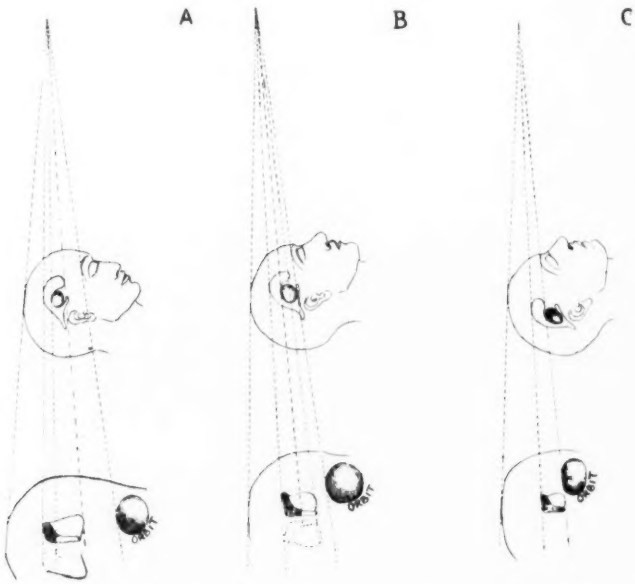

Fig. 7.—Projection of roentgen rays from a tube on an imaginary plate: *A*, with head forward, *B*, erect, and *C*, backward, to show the change in shadow pattern.

Shadow 3 (fig. 2).—This shadow is due to the total length of the upper portion of the body of the ventricle, and therefore always appears darker than the rest of the shadows, as this is the longest air-filled space in the picture, particularly with the partial overlapping of portions *2* and *4*. Shadow *3* is clearly indicated in the frontal section of the brain in figure 8, and the line which separates *3* from *2* is seen to be the upper surface of the thalamus. It is bounded laterally by the body of the caudate and above by the corpus callosum. If the ventricle is filled with air back to and including portion *3*, the resultant shadow formed by portions *1*, *2* and *3* is that seen in the sketch immediately above the brain

in figure 8. When the ventricle is completely filled with air, the additional shadows *4*, *5* and *6* can be seen as in figure 9.

Shadow 4 (fig. 2).—This shadow is produced by the posterior portion of the body which curves backward, downward and laterally; com-

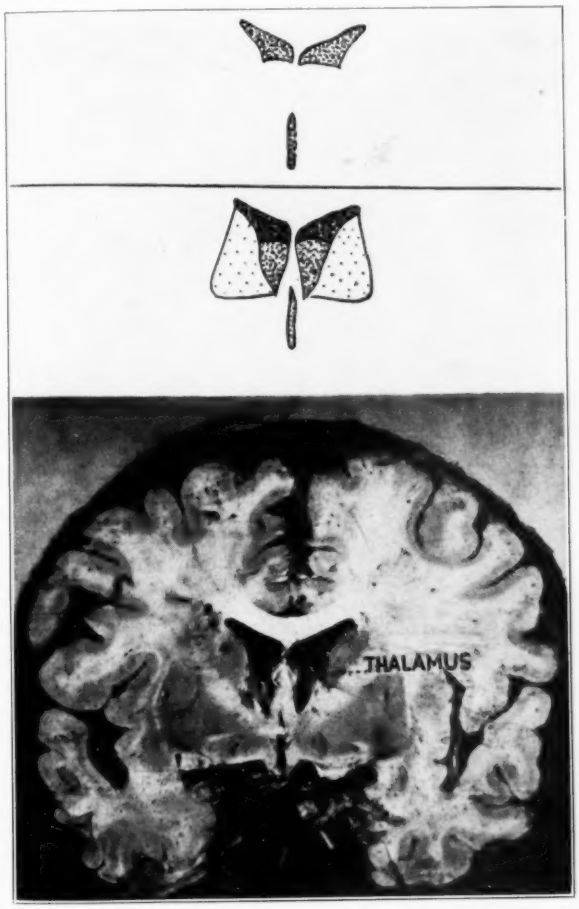

Fig. 8.—Frontal section through the brain through the posterior part of portion *2*.

pare figures *2*, *5*, *9* and *10*. If the whole ventricular system is filled, and anteroposterior roentgenograms are taken with brow up and plate below occiput, the distorting magnification makes the anterior horns appear to extend from the midline a distance at least equal to that of portion *4* as indicated in figure 9. The true relationship of portion *2* to portion *4* is shown in figure 5.

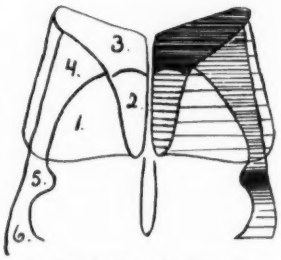

Fig. 9.—Superposition of ventricular shadow in an anteroposterior plate.

Fig. 10.—Ventricular model in anteroposterior view.

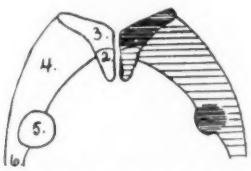

Fig. 11.—Superposition of ventricular shadow in postero-anterior plate.

Fig. 12.—Ventricular model in postero-anterior view.

Shadow 5 (fig. 2).—This is cast by the posterior horn and is consequently not constantly seen, because the posterior horn is quite often lacking even when the ventricles are normal.[5] It usually appears as a dark, circumscribed shadow which is superimposed on and lies between shadows *4* and *6*, and usually projects somewhat mesially (figs. 11 and 12).

Shadow 6 (fig. 2).—The shadow appears at a still lower level than shadow *5* and represents the inferior horn. The extreme tip of the inferior horn is rarely seen when the occiput is up because of the pooling of fluid in it. On the other hand, when the brow is up, only the tip may be seen, frequently outlined by the orbit. Its relationships may be seen in figures 9 to 12. The appearance seen in an anteroposterior view may be compared with that in a postero-anterior view by reference to figures 9 and 11, and corresponding views of the model are added in figures 10 and 12.

LATERAL VIEW

The general outlines of the ventricles seen from the side are easily understood. It should be repeated that adequate oscillation and posturing of the head is even more important in these views so that the anterior, posterior or inferior horn may be completely filled according to the clinical indications, and that the confusing half-truths of partial filling may be avoided.

A helpful aid to successful posturing is the use in the x-ray room of a model such as that shown in figure 1. The subarachnoid cisterns [5] must be recognized. The interpeduncular cistern often overlies the inferior horn, but is easily recognized by its triangular shape. The general outline of the lateral ventricle follows that of the skull, so that a ventricle of a brachycephalic skull is shorter and more sharply curved than that of a dolichocephalic skull.

In general it may be observed that the lateral ventricle outlines the thalamus between its body and the inferior horn. The rather deep but variable notch seen dorsally between body and posterior horn is the impress of the splenium of the corpus callosum. Narrowing or absence of the posterior horn is not to be considered an abnormality. The outline of the foramen of Monro is usually seen at the postero-inferior angle of portion *2* of the lateral ventricle.

The third ventricle is easily recognized by its standard anatomic form and position. If not filled in the lateral view taken with brow up, it may often be demonstrated by a lateral view with chin uppermost.

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5. Penfield, W. G.: Cerebral Pneumography, Arch. Neurol. & Psychiat. **13:** 580 (May) 1925.

The aqueduct of Sylvius and the fourth ventricle are likewise easily seen, and the sharply triangular shape of the latter is distinctive. It may be borne in mind that the aqueduct runs vertically when the head is erect.

TECHNIC OF INSUFFLATION

Spinal insufflation for diagnostic purposes has come to be described in neurologic parlance as encephalography. Many variations in technical procedure have been described.[6] Ordinarily, the injection is made with the patient in the sitting position. The head should be tipped slightly forward to keep the gas out of the basal cisterns and to promote its entrance into the fourth ventricle. Occasionally no air enters the ventricular system. In our clinic Dr. Cone has devised a maneuver which tends to prevent such failures: He injects 10 cc. of air before removing any fluid; this seems to prevent the collapse of the portals of entry in question.

Following the spinal injection of air there is usually observed a mild rise in temperature during the succeeding twenty-four hours. This we have observed in the majority of the cases to be associated with the appearance of white and sometimes red blood cells in the urine. Our attention was called to this matter six years ago at the Presbyterian Hospital, where in two cases pyelitis followed spinal insufflation of air.

The mechanism of this phenomenon requires further study. Absorption of the subarachnoid air is ordinarily very rapid, going on to disappearance of large quantities within the first few hours. The plates of the second day usually show air only in the ventricles. One may conjecture that the unabsorbable portion of the air appears in the cerebral sinuses in minute bubbles which have a direct effect on the small capillaries of the kidney when they reach them.

Because of this effect of air and because of the headache and increase of pressure that follow its use, we have in our clinic largely used oxygen in the past three years for diagnostic purposes. Oxygen is taken into a sterile rubber bag provided with a stopcock and is then filtered, as needed, through a tube containing cotton wool. It was evident at once that headaches following injection became definitely less intense, and that the disappearance of the gas from the cranial cavity was very much hastened. It seemed probable that the urinary irritation of oxygen was much less than that of air, according to work which Dr. Maurice Brodie began while he was in our service.

Spinal insufflation for the treatment of posttraumatic headache[7] should be carried out with air, however, and not with oxygen, as the longer retention of the gas within the cranial cavity is under such circumstances desirable.

In carrying out a spinal insufflation for this purpose, the model which we have described in figure 1 has proved of great help. The aim in such a procedure is to induce the air to pass into the subarachnoid space without any of it entering the ventricles. Furthermore, the air must be allowed to pass to that area of the skull where the pain is felt.

The lumbar puncture should be carried out with the patient lying on his side and the head of the table somewhat elevated. The head is rotated partially upward so as to provide for passage of the air into the basal cisterns and thus over the convexity of the brain on the side on which the headache is felt. The use of the

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6. Bingel, A.: Klin. Wchnschr. **19**:637, 1922. Liberson, F.: Am. J. Roentgenol. **15**:231, 1926. Waggoner, R.: Am. J. M. Sc. **174**:459, 1927.

7. Penfield, W.: Surg., Gynec. & Obst. **45**:747, 1927.

model makes the proper position of the head apparent at once. If the neck is sharply flexed downward the aqueduct of Sylvius can be made to slope somewhat downward, instead of upward, to the third ventricle; this prevents the passage of bubbles into the ventricular system but still allows them to pass forward in the basal cisterns and upward and outward in the fissure of Sylvius. It is better not to use too much air. Seventy-five cubic centimeters should be adequate, and the effort should be made to compress the hemispheres slightly by the presence of the air and to allow the ventricles to collapse somewhat. The patient is then kept in position with the painful area of the skull uppermost, and the head is oscillated in one or the other direction every minute for a period of from thirty to sixty minutes so that the bubble of air may pass freely backward and forward between the skull and the hemisphere.[8]

In direct ventricular injections, as well as in diagnostic spinal insufflation, oxygen is to be preferred to air for the reasons already given. In case there is greatly increased pressure, operation should usually be carried out the same day, a precaution which has been adopted, no doubt, in most neurosurgical clinics to prevent the fatalities which sometimes occur from increase of pressure in the closed skull following ventricular injection.

SUMMARY

This communication discusses only certain aspects of the subject which interest us, and does not describe in detail those aspects of it which are obvious and therefore uninteresting. The model which we present will be found of use both for ventriculographic interpretation and during the technical procedure involved.

Pneumographic interpretation should be carried out by those who understand the clinical problems. The head must be placed in such a position as to fill completely with gas those portions of the ventricle in question. Partial filling is a fruitful source of misinterpretation. Oxygen instead of air for diagnostic purposes is safer and gives greater comfort to the patient.

Anterior horn, body and posterior horn are vague terms. We have therefore divided the lateral ventricle, as seen from the side, into six portions. Each of these portions may be readily recognized as a unit in anteroposterior view, and the structures which give them their peculiar outlines identified (figs. 2 and 9). Such an analysis renders the detection and description of departures from normal a relatively simple procedure.

DISCUSSION

Dr. Francis C. Grant (Philadelphia): This study is important because it shows exactly which part of the air-filled ventricles is responsible for the various shadows seen on the roentgen film. The model demonstrated is of value in illus-

8. In our experience the use of $\frac{1}{200}$ grain (0.0003 Gm.) of scopolamine hydrobromide and $\frac{1}{8}$ grain (0.008 Gm.) of morphine fifteen minutes before the injection, and the same medication repeated at the beginning of the injection, takes away a large part of the pain associated with the procedure and may make the period of oscillation quite free from discomfort.

trating the relationship between the normal ventricles and the cranial bones. However, in encephalograms of what have been considered normal ventricles, I have seen shadows somewhat different from those here exhibited. There is a lateral shadow which extends well out beyond what the authors have termed "portion 1" and, I believe that this is due to the presence of air in the inferior ventricular horn. It may be that this difference is due to incomplete drainage and consequent lack of air in this region in the films that Dr. Torkildsen has shown. We take great pains to obtain complete drainage and this, I believe, is the reason for our ability to demonstrate this lateral shadow which is the inferior horn, the most difficult area of the ventricular lakes to drain completely.

There are two other minor points that are worth emphasizing. First, if drainage is complete, the choroid plexus can be seen as a filling defect in the floor of the lateral ventricles in properly taken anteroposterior views. In lateral views a similar filling defect due to the choroid may be seen in the fourth ventricle. Second, in the lateral films, the upper edges of the shadows produced by air in the anterior and posterior horns of the lateral ventricle never seem to overlap exactly. One edge is always lower than the other. Attention is drawn to these two minor details because an inexperienced observer might mistake the small defect caused by the choroid for a tumor, or the fact that the upper edge of the ventricular shadows are not symmetrical might lead him to believe that the lower one had been depressed by a tumor. However, I do not believe that it is through the medium of these minor changes in encephalographic outline that tumors of the brain are localized. Such lesions always produce more obvious defects in the size, shape and position of the ventricles.

We have taken roentgen films of patients, twenty-four, forty-eight, seventy-two and ninety-six hours after encephalography. The air finally seems to collect in a blob over one cortex or the other, disappearing from the ventricles and from the subarachnoid space in other areas. I believe that this air is in the subdural space, but I cannot explain how it leaves the subarachnoid space. Does Dr. Torkildsen agree that this residual air is in the subdural space? If so, how does it reach this position?

DR. TEMPLE FAY (Philadelphia): I believe that the authors have called attention to a most important fact that was stressed about four years ago by the Commission on the Interpretation of Encephalography. Dr. Pancoast and Dr. Pendergrass at that time definitely established that in order to prevent distortion the tube distance had to be at least 44 inches (111 cm.). Since that time Dr. Chamberlain has shown that by using a fine focus tube and a fixed and automatically adjustable head rest every patient is taken in the exact anteroposterior position.

As Dr. Penfield and Dr. Torkildsen have pointed out, by using a fine focus tube and by having the patient in a proper position, it is possible to trace the walls of the ventricle through stereoscopic vision, so that Dr. Chamberlain has been able to show small tumor projections that we had not been able to see before. We have seen the defects produced by softening in the region of the thalamus and ventricular wall which it was impossible to see three or four years ago. Dr. Penfield's work is extremely important from that angle.

The point that Dr. Grant brought up is important and has been under discussion for a long time. I may add that he has shown films with subdural air. I can be sure of this because I have had reason to verify the fact by trephining within eighteen hours after the making of an encephalogram with such an indication, and I have also had the opportunity of injecting subdural air by an opening in the temporal area and of deliberately introducing air under the dura. This procedure gave a picture similar to that shown in the last film.

The question as to how that air passes from the subarachnoid space into the subdural space is a matter which demands a good deal of investigation and consideration.

DR. WILDER PENFIELD (Montreal, Canada): It is all very well to assume that the ventricles are well known anatomic structures. In spite of that apparent fact the literature is full of perfectly obvious mistakes in ventriculographic interpretation. The mistake most frequently made in the anteroposterior views is to assume that portions *2* and *3* represent the anterior horn. The most anterior part of the lateral ventricles is portion *1*. This portion passes downward and laterally as well as forward. Because of its lateral deviation and its thinness it casts a very thin shadow, and so comes to be ignored. The x-ray technician is apt to contribute to this mistake as follows: As the plate is developing he catches sight of portions *2* and *3* and develops the film so as to lose the thin portion *1* almost altogether. Thereupon the interpreter assumes that the butterfly shape really represents the anterior horn. On the following day, however, the technician, when he is developing his plates and looking for air in them, sees this very thin portion, as portions *2* and *3* have now disappeared. The disappearance of portions *2* and *3* is, of course, due to the fact that the air in them has been absorbed, leaving only the most anterior portion of the ventricle filled, with the brow up. He therefore develops his plates in such a way as to bring out this thin shadow as intensely as possible. The interpreter may then be led to assume that the ventricle has changed its shape. He now sees the air placed more laterally, the outline is rounded, and the butterfiy outline has disappeared; he may be misled into believing that the ventricle has become enlarged.

The question of subdural air was not touched on in our paper. Dr. Grant has therefore brought up a new and interesting problem. I believe that the shadows which Dr. Grant showed represent subdural air, although I know that the nature of these shadows is open to discussion. It must be borne in mind, of course, that when there is cortical atrophy the subarachnoid fissures are deeper than usual; a plate may then show a great deal of air near the midline and over the convexity of the hemisphere which resembles subdural air, but which in reality is only subarachnoid air in wide channels. I am certain that, as Dr. Fay believes, in some cases air does pass into the subdural spaces. I cannot say how it gets there. There seem to be only two possibilities: One is that there was an opening between the subarachnoid and the subdural space before the injection was made. The other is that the presence of the air has caused a breaking through into the subdural space.

I know from the study of a large series of animals that normally the subdural and subarachnoid spaces are quite separate and that the subdural space contains fluid with a yellowish tinge, whereas the subarachnoid fluid is colorless. It is our experience that the air appears in the subdural space clinically much more frequently in cases of posttraumatic meningeal headache than in other cases. We had thought that possibly this fact bore relation to the cause of the headache in certain cases.

Dr. Fay has mentioned the importance of position in roentgen examination. We agree that it is important to standardize positions and measurements. I believe that he favors the taking of all plates with the patient sitting in the erect position. We prefer, as a rule, to have the patient lying in the horizontal position, because of the fact that the all-important thing in ventriculography is to fill completely that portion of the ventricle which one wishes to study. This can best be done with either the brow or the occiput uppermost. It is dangerous to standardize the procedure too completely; every case presents a different prob-

lem. When we take routine plates, we prefer always to have the patient lying horizontally, but this may be largely a personal preference. Finally, we have made no attempt to outline complete rules for interpretation.

We present a model which will be found useful and point out the identity of the various portions of the shadows seen in an anteroposterior plate, and we make certain technical suggestions.

DR. ARNE TORKILDSEN (Montreal, Canada): I should like to answer Dr. Grant's question. He asked why we do not see more of the inferior horn on our sketches. I think the all-important fact here is the position of the head. If the head is kept in a fairly erect position, the longitudinal axis of the inferior horn will become more or less parallel to the axis of the roentgen rays. Consequently the inferior horn will be shortened very much and seen, not as a long projecting arm downward, but only as a very short tip. It is difficult to decide where the posterior part of the ventricle ends and where the inferior horn begins. I do not think that this can be done exactly unless the posterior horn is present and indicates its position by a dark circumscribed area.

ANATOMIC AND FUNCTIONAL RELATIONSHIPS OF THE NUCLEUS DORSALIS (CLARKE'S COLUMN)

AND OF THE DORSAL SPINOCEREBELLAR TRACT (FLECHSIG'S)

ISADORE J. PASS, M.D.
MINNEAPOLIS

The functional significance of the nucleus dorsalis, its relationship to incoming fibers and the course and termination of the fibers arising from its cells have been the subject of controversial discussions since Clarke's [1a] description of the nucleus in 1851.

It was early demonstrated that the nerve endings ramifying about the cells of Clarke's column come from fibers of the dorsal nerve roots which swing into the posterior column. These fibers were interpreted by Gaskell [2] as being visceral rami. He showed that the visceral rami were limited to three regions of the central nervous system: (1) a cervicocranial region, (2) a thoracic region and (3) a sacral region. Then he pointed out that Clarke's column forms a discontinuous column, the cell groups of which correspond accurately to those regions. He said: "The connection of these fibers with this column of cells is to my mind proved conclusively by the fact that the cells of Clarke's column are confined to those regions of the central nervous system which give origin to the rami viscerales." However, Gaskell admitted that "the rami viscerales have not been directly traced into the cells of the columnae vesiculares" [Clarke's columns]. Edgeworth [3] also was impressed by the fact that the "limits of origin [of the visceral sensory fibers] from the spinal cord, and their quantitative distribution within these limits, bear a striking resemblance to that of the cells of Clarke's column."

Other workers concluded from experimental evidence that the central endings about Clarke's column were visceral fibers. Thus Biedl,[4] on cutting the splanchnic nerves of dogs, found chromatolytic

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This investigation was undertaken at the suggestion and carried out under the direction of Dr. A. T. Rasmussen, Professor of Neurology, Department of Anatomy, University of Minnesota Medical School.

1. Clarke, J. L.: (*a*) Researches into the Structure of the Spinal Cord, Phil. Tr. Roy. Soc. London **141**:607, 1851; (*b*) Researches on the Intimate Structure of the Brain, ibid. **158**:26, 1868.

2. Gaskell, W. H.: On the Structure, Distribution and Function of the Nerves Which Innervate the Visceral and Vascular Systems, J. Physiol. **7**:1, 1886.

3. Edgeworth, F. H.: On a Large-Fibred Sensory Supply of the Thoracic and Abdominal Viscera, J. Physiol. **13**:260, 1892.

4. Biedl, A.: Ueber die Centra der Splanchnici, Wien. klin. Wchnschr. **8**: 915, 1895.

changes in many areas of the spinal cord, notably in Clarke's column. Onuf and Collins [5] performed three types of experiments: extirpation of the stellate ganglion, removal of the lower part of the thoracic sympathetic chain with the corresponding ganglia and removal of a part of the lumbar ganglionic chain. For the investigation of sensory fibers they used the Marchi method. They believed that they had furnished, through their experiments, proof that the visceral sensory fibers come in contact with the cells of Clarke's column and with the large cells of the pars intermedia, which includes the gray matter between Clarke's column and the lateral horn. Kohnstamm and Wolfstein,[6] as a result of their investigation of this problem, arrived at similar conclusions. Laignel-Lavastine [7] extirpated the sympathetic chain in dogs. This caused cytolysis, pyknosis and atrophy of the cells of the lateral horn, of the paracentral group, of the pars intermedia and of Clarke's column. Three experiments were reported. In the second of these, Marchi degeneration was described in the posterior columns and in Clarke's columns. However, these experiments can hardly be considered conclusive, because hemorrhages, which might well have been responsible for the destruction of the cord, were found in the gray matter.

These results, moreover, could not be confirmed by Nottebaum,[8] Huet,[9] Lapinsky and Cassirer [10] or, more recently by Bok.[11] Lapinsky and Cassirer suggested that the difficulty may lie in the interpretation of histologic structure. In the pars intermedia cells are normally present the chromatic condition of which is similar to that described following experimental lesions of the preganglionic fibers. The condition of these cells, said Bielschowsky,[12] reminds one remarkably of the picture of retrograde ganglion cell changes as they regularly occur after section of the axis-cylinder of the corresponding cell.

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5. Onuf, B., and Collins, J.: Experimental Researches on the Localization of the Sympathetic Nerve in the Spinal Cord and Brain, and Contributions to Physiology, J. Nerv. & Ment. Dis. **25**:661, 1898.

6. Kohnstamm, O., and Wolfstein, J.: Versuch einer physiologischen Anatomie der Vagusursprünge und des Kopfsympathicus, J. f. Psychol. u. Neurol. **8**:177, 1907.

7. Laignel-Lavastine, M.: Note sur quelques centres sympathiques de la moelle épinière, Rev. neurol. **12**:885, 1904.

8. Nottebaum, J.: Ueber die sekundäre Degeneration nach Durchschneidung des Halssympathicus, Inaug. Dissert., Marburg, J. Hamel, 1897, p. 1.

9. Huet, W. G.: De gevolgen der exstirpatie van het ganglion supremum colli nervi sympathici voor het centrale zenuwstelsel, Dissert, Utrecht, 1898.

10. Lapinsky, M., and Cassirer, R.: Ueber den Ursprung des Halssympathicus im Rückenmark, Ztschr. f. Nervenheilk. **19**:137, 1901.

11. Bok, S. T.: De centrale verhoudingen van den nervus sympathicus, Nederl. tijdschr. v. geneesk. **66**:642, 1922.

12. Bielschowsky, M.: Nervengewebe, Handbuch der mikroskopischen Anatomie des Menschen, Berlin, Julius Springer, 1928, vol. 4, pt. 1, p. 34.

Most investigators have believed that the nerve endings about the cells of Clarke's column are somatic afferent. This view gained credence following the observations of Lissauer,[13] Sottas,[14] Redlich,[15] Mayer[16] and others, who showed that Clarke's column in the region of its greatest development receives fibers from the posterior roots of the lower lumbar and perhaps also from those of the sacral region of the spinal cord. Obviously the lower lumbar nerves can convey but few visceral sensory fibers to the central nervous system.

It has been argued by some investigators, following the leadership of Gaskell, that Clarke's column must be a visceral sensory nucleus because it corresponds accurately to those regions of the central nervous system to which afferent visceral rami are limited. However, Clarke's column is not at all as sharply demarcated as Gaskell supposed (Hollis[17a]). Hollis demonstrated the existence of cells of Clarke's column even in the filum terminale of the human cord. Scharcherl[18] showed that in man Clarke's column often forms an unbroken column of cells from the first cervical to the fifth sacral segment. This fact was recently confirmed by Massazza.[19]

Gaskell[2] traced the upper end of Clarke's column into the sensory nuclei of the vagus and glossopharyngeal nerves. These, he said, not only are situated "in the proper position for the continuation of Clarke's column, but also are composed of the same kind of cells as that column." Johnston,[20] on the basis of comparative studies, agreed that the solitary fasciculus and its nucleus become continuous with the upper end of Clarke's column. Other investigators, however, traced Clarke's column into the nucleus cuneatus, especially into its external portion, known as von Monakow's nucleus (magnocellularis). This connection was first postulated by Hollis,[17a] who pointed out the similarity of the cells in the two nuclei. The similarity in size, shape and staining proper-

13. Lissauer, H.: Beitrag zum Faserverlauf im Hinterhorn des menschlichen Rückenmarks und zum Verhalten desselben bei Tabes dorsalis, Arch. f. Psychiat. **17**:377, 1886.

14. Sottas, J.: Contribution à l'étude des dégénérescences de la moelle consécutives aux lésions des racines postérieures, Rev. de méd., Paris **13**:290, 1893.

15. Redlich, E.: Pathologie der tabischen Hinterstrangserkrankung, Jena, Gustav Fischer, 1897, pp. 25 and 91.

16. Mayer, C.: Zur pathologischen Anatomie der Rückenmarkshinterstränge, Jahrb. f. Psychiat. u. Neurol. **13**:57, 1895.

17. Hollis, W. A.: (*a*) Researches into the Histology of the Central Grey Substance of the Spinal Cord and Medulla Oblongata, J. Anat. & Physiol. (pt. 2) **18**:62, 1884; (*b*) ibid. **17**:517, 1883.

18. Scharcherl, M.: Ueber Clarke's "Posterior Vesicular Columns," Arb. a. d. Neurol. Inst. a. d. Wien. Univ., 1902, p. 314.

19. Massazza, A.: La citoarchitettonica del midollo spinale umano. Nota preventiva, Riv. di pat. nerv. **28**:22, 1924.

20. Johnston, J. B.: The Nervous System of Vertebrates, Philadelphia, J. B. Lippincott Company, 1906, p. 155.

ties of the two groups of cells was noted also by Sherrington,[21] by Blumenau [22] and, recently, by Gagel and Bodechtel.[23]

The problem of the course and termination of the fibers arising from Clarke's column has also presented highly controversial aspects ever since the discovery of the nucleus. In 1872, Gerlach [24] succeeded in demonstrating in gold preparations sharply demarcated bundles of fibers coming from Clarke's column and extending outward toward the lateral funiculus. This relationship was definitely proved by Pick,[25] in 1878, when he was able to trace processes from the cells of Clarke's column to the lateral funiculus in the upper lumbar region of the cord of a child aged 6 months. This was later confirmed by Ramón y Cajal [26] in Golgi preparations of the cord of a new-born mouse. Flechsig [27] was the first to surmise a connection between Clarke's column and the dorsal spinocerebellar tract. Subsequent investigators have with only few exceptions corroborated Flechsig's observations, concluding that the dorsal spinocerebellar tract arises from the cells of Clarke's column (Edinger,[28] Auerbach,[29] Bechterew,[30] Mott,[31a, b]

21. Sherrington, C. S.: On Outlying Nerve Cells in the Mammalian Spinal-Cord, Phil. Tr. Roy. Soc. London, B, **181**:33, 1890.

22. Blumenau, L.: Ueber den äusseren Kern des Keilstranges im verlängerten Mark, Neurol. Centralbl. **10**:226 and 589, 1891.

23. Gagel, O., and Bodechtel, G.: Die Topik und feinere Histologie der Ganglienzellgruppen in der Medulla oblongata und im Ponsgebiet mit einem kurzen Hinweis auf die Gliaverhältnisse und die Histopathologie, Ztschr. f. Anat. u. Entwcklngsgesch. **91**:178, 1930.

24. Gerlach, J.: The Spinal Cord, in Stricker, S.: [illegible]al of Human and Comparative Histology, translated by Henry Power, London, New Sydenham Society, 1872, vol. 2, p. 359.

25. Pick, A.: Zur Histologie der Clarke'schen Säulen im menschlichen Rückenmarke, Centralbl. f. d. med. Wissensch. **16**:20, 187[illegible]

26. Ramón y Cajal, S.: Histologie du [illegible] de l'homme et des vertébrés, Paris, A. Maloine, 1909, vol. 1,

27. Flechsig, P.: Die Leitungsbahnen im Gehirn und Rückenmark des Menschen auf Grund entwicklungsgeschichtlicher Untersuchungen dargestelt, Leipzig, Wilhelm Engelmann, 1876, p. 291.

28. Edinger, L.: Vergleichend-entwicklungsgeschichtliche und anatomische Studien im Bereiche des Centralnervensystems: II. Ueber die Fortsetzung der hinteren Rückenmarkswurzeln zum Gehirn, Anat. Anz. **4**:121, 1889.

29. Auerbach, L.: Zur Anatomie der aufsteigend degenerierenden Systeme des Rückenmarks, Anat. Anz. **5**:214, 1890.

30. Bechterew, W.: Ueber die Erscheinungen welche die Durchschneidung der Hinterstränge des Rückenmarkes bei Tieren herbeiführt und über die Beziehungen dieser Stränge zur Gleichgewichtsfunction, Arch. f. Physiol. 1890, p. 489.

31. Mott, F. W.: (*a*) Ascending Degeneration Resulting from Lesions of the Spinal Cord in Monkeys, Brain **15**:215, 1892; (*b*) Experimental Enquiry upon the Afferent Tracts of the Central Nervous System of the Monkey, ibid. **18**:1, 1895; (*c*) The Bi-Polar Cells of the Spinal Cord and Their Connections, ibid. **13**:433, 1890; (*d*) Microscopical Examination of Clarke's Column in Man, the Monkey and the Dog, J. Anat. & Physiol. **22**:479, 1888.

Schäfer,[32] Lewandowsky,[33] Marburg,[34] Schäfer and Bruce,[35] Bing,[36] Thomas[37] and Obersteiner[38]).

On the other hand, there is complete lack of agreement on the question as to whether these fibers are crossed or uncrossed. Edinger[28] and Pellizi[39] thought that all the fibers of the dorsal spinocerebellar tract are crossed; Auerbach,[29] Bechterew[30] and Schäfer[32] believed that the fibers are uncrossed; Mott,[31a,b] Lewandowsky,[33] Schäfer and Bruce[35] and MacNulty and Horsley[40] believed that there is partial crossing of the tract, while Bing,[36] Thomas[37] and Horrax[41] stated that the majority of fibers cross.

The general course of the dorsal spinocerebellar tract in the central nervous system was demonstrated to the satisfaction of most observers by the investigations of Mott,[31] and has been more recently confirmed by Beck.[42] However, there has been but little agreement concerning the termination of the dorsal spinocerebellar tract in the cerebellum. MacNulty and Horsley,[40] Ingvar[43] and Beck,[42] however, were of the opinion that the dorsal spinocerebellar tract ends in the superior, middle

32. Schäfer, E. A.: Some Results of Partial Transverse Section of the Spinal Cord, (Proc. Physiol. Soc. London, March 18, 1899), J. Physiol. **24**:XXII, 1899.

33. Lewandowsky, M.: Untersuchungen über die Leitungsbahnen des Truncus Cerebri und ihren Zusammenhang mit denen der Medulla spinalis und des Cortex Cerebri, Denkschr. d. med.- Naturwissensch. Gesellsch. z. Jena **10**:98, 1904.

34. Marburg, O.: Die physiologische Function der Kleinhirnseitenstrangbahn (Tractus spinocerebellaris dorsalis) nach Experimenten am Hunde, Arch. f. Physiol., (supp. vol.), 1904, p. 457.

35. Schäfer, E. A. and Bruce, A. M.: The Cerebellar Tracts of the Spinal Cord, (Proc. Physiol. Soc. London, May 18, 1907), J. Physiol. **35**:XLIX, 1907.

36. Bing, R.: Die Bedeutung der spinozerebellaren Systeme, Wiesbaden, J. F. Bergmann, 1907.

37. Thomas, [illegible] Cerebellar Functions, translated by W. C. Herring, Monograph Series, Washington, D. C., Nervous and Mental Disease Publishing Company, 1.

38. Obersteiner, H.: Anleitung beim Studium des Baues der nervösen Zentralorgane im gesunden und kranken Zustande, ed. 5, Vienna, Franz Deuticke, 1914.

39. Pellizi, G. B.: Sur les dégénérescences secondaires dans le système nerveux central, à la suite de lésions de la moelle et de la section de racines spinales. Contribution à l'anatomie et à la physiologie des voies cérébelleuses, Arch. ital. de biol. **24**:89, 1895.

40. MacNulty, A. S., and Horsley, V.: On the Cervical Spinobulbar and Spinocerebellar Tracts and on the Question of Topographical Representation in the Cerebellum, Brain **32**:237, 1909.

41. Horrax, G.: A Study of the Afferent Fibers of the Body Wall and of the Hind Legs to the Cerebellum of the Dog by the Method of Degeneration, Anat. Rec. **9**:307, 1915.

42. Beck, G. M.: The Cerebellar Terminations of the Spinocerebellar Fibers of the Lower Lumbar and Sacral Segments of the Cat, Brain **50**:60, 1927.

43. Ingvar, S.: Zur Phylo- und Ontogenese des Kleinhirns, Folia Neurobiol. **11**:205, 1918.

and inferior vermis of the same side, while a small number of fibers enter the hemisphere and the stalk of the flocculus, also on the same side.

MATERIAL AND METHODS

Various procedures were undertaken, such as the injection of silver nitrate in various concentrations and of distilled water into the nucleus dorsalis, making incisions between the two nuclei, sectioning the dorsal roots at various levels and studying the histologic picture of the nucleus dorsalis both before and after experimental cauterization of the dorsal spinocerebellar tract.

Adult cats were anesthetized with avertin (300 mg. per kilogram of body weight).[44] The level for entering the spinal canal was located by palpating the spinous processes of the vertebrae. The seventh lumbar spine is very prominent and affords a convenient landmark. The site of operation was shaved and prepared with iodine and alcohol. For injections into the nucleus dorsalis a C-shaped incision was made through the skin, and the skin flaps were retracted. Then two longitudinal incisions were made through the lumbodorsal fascia parallel and close to the spinous processes. The sacrospinalis muscles were bluntly dissected back from the laminae and pushed over the transverse processes. The spinous process of the vertebra at the level selected was pinched off, and a circular disk was removed from the lamina by means of a trephine. This exposed the extradural fat, which was pushed aside to bring into view the dura mater. The dura was grasped with a fine forceps, and a longitudinal incision was made in it with a fine iridectomy knife. The midline of the spinal cord is well marked by the posterior longitudinal artery.

The apparatus used for making injections into Clarke's column consists of a dissecting microscope of the type that can readily be adjusted in all directions (fig. A). In the clip of the apparatus was inserted an empty spool, to the top of which was attached a celluloid cup. About a dozen turns of 26-gage brass wire were sewed into the celluloid cup. The brass wire was connected by means of copper leads to an alternating current transformer with a sliding contact. A single-throw switch was inserted in one of the leads. A capillary pipet, made by blowing out one end of a glass tube to form a bulb and drawing out the other end to a very fine tip, was inserted through the celluloid cup and through the spool so that the bulb of the pipet fitted into the celluloid cup (fig. A). The pipet was filled by inserting its tip into the solution used for injection; the capillary attraction caused sufficient fluid to be drawn up. The sliding contact of the transformer was adjusted to furnish the current necessary to heat gently the brass wire about the bulb. The apparatus was then put in place, and the main screw of the stand was turned so that the pipet descended perpendicularly, just laterally to the midline and to the desired depth, into the spinal cord of the animal used in the experiment. Then the switch was thrown. The heat generated by the resistance in the brass wire caused the air in the glass bulb to expand, thus forcing the solution into the spinal cord without disturbing the position of the pipet.

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44. The advantages of avertin in experimental operations on the brain have been summarized recently by Rasmussen, G. L.: Avertin as an Anesthetic during Experimental Operations on the Nervous System of the Cat, Proc. Soc. Exper. Biol. & Med. **29**:283, 1931.

The material used for injection was principally a 25 per cent solution of silver nitrate. Silver nitrate was chosen because it was thought that this compound would be immediately precipitated by the chlorides in and about the nerve cells, thus preventing diffusion of the caustic. In this manner it was hoped that small, well circumscribed lesions might be made. However, the 25 per cent solution of silver nitrate proved too destructive, so 12.5 and 10 per cent concentrations were used in the later experiments. Distilled water was also used, since it is supposed to act selectively, destroying only cells, apparently by surrounding them with an extremely hypotonic solution. In a few instances no injection material was used. A midsagittal incision between the two columns was also attempted.

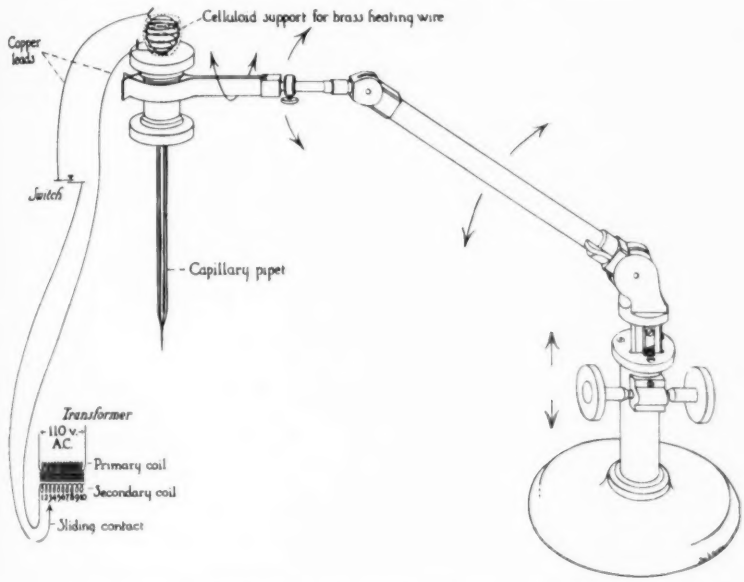

Fig. A.—Apparatus used for injections into Clarke's column.

It was deemed advisable to restudy the relationship of the incoming fibers of the dorsal root to Clarke's column by cutting one or more dorsal roots between the ganglion of the dorsal root and the spinal cord in several cats.

The animals were killed twelve days after operation. The brain and spinal cord were removed and handled by the Marchi method (Rasmussen[45]). Twenty animals survived sufficiently long to be useful. The dorsal roots were cut in seven, injection with a 25 per cent solution of silver nitrate was attempted in five, injection with a 12.5 per cent solution of silver nitrate in two, injection with a 10 per cent solution of silver nitrate in two, injection with distilled water in two and insertion of the pipet without injection in two.

The cytologic characteristics of the cells of the nucleus dorsalis and of similar cells found in the nucleus cuneatus were studied in human material stained by the Nissl method.

45. Rasmussen, A. T.: Secondary Vestibular Tracts in the Cat, J. Comp. Neurol. **54**:143, 1932.

RESULTS

1. *The Relations of the Fibers of the Dorsal Root to Clarke's Column.*—In order to determine the relationship of the fibers of the dorsal root to Clarke's column, the dorsal roots of the sacral nerves of the left side were severed in cat 85. The animal recovered from the effects of the operation, and at the time it was killed appeared normal except for a slight weakness of the left hindleg, which tended to bow laterally as the animal walked. Marchi preparations of the cord of this animal showed degenerated fibers extending into Clarke's column of the same side as high as the second lumbar segment of the cord, that is, six segments above the level of the dorsal roots cut (figs. 4 and 5). In cat 89 the dorsal roots of the seventh lumbar and of the first sacral nerves were cut. In this animal it was possible to trace degenerated fibers as high as the first lumbar level, again six segments above the level of the highest dorsal root destroyed (figs. 1, 2 and 3). These findings are in accord with observations made on man. Thus, Mayer [16] described a case in which Clarke's column received, in the region of its greatest development, numerous fibers from the four posterior lumbar dorsal roots. Similarly, Sottas [14] showed that lesions in the region of the cauda equina regularly result in degeneration in Clarke's column far up into the thoracic cord. In apes and in dogs, Mott [31c] showed that after section of the dorsal roots of the cauda equina there results a considerable degeneration of the collaterals to Clarke's column in the thoracic cord. It is hardly logical to assume that all these sensory fibers coming from the lower extremities and ending about Clarke's columns are visceral. Obviously, there are but few visceral sensory fibers in the extremities. Therefore, one must conclude that these are proprioceptive, and because the impulses conveyed eventually reach the cerebellum they must be unconscious proprioceptive fibers. This point of view is corroborated further by the work of Lissauer,[13] Krauss,[46] Oppenheim,[47] Siemerling [48] and others, who claimed that in locomotor ataxia there is early atrophy of the fine nerve plexus surrounding Clarke's columns.

Gaskell [2] insisted on the existence of a connection between Clarke's column and the visceral rami because the groups of cells of the column, according to him, correspond accurately with the extent of these fibers. In an attempt to verify this contention, the dorsal roots of the thoracic nerves were cut in several animals. In cat 103 the left dorsal root of

46. Krauss, E.: Zur pathologischen Anatomie der Tabes dorsalis, Neurol. Centralbl. **4**:49, 1885.

47. Oppenheim, H.: Neue Beiträge zur Pathologie der Tabes dorsalis, Arch. f. Psychiat. **20**:131, 1889.

48. Siemerling, E.: Zur Lehre von der congenitalen Hirn- und Rückenmarkssyphilis, Arch. f. Psychiat. **20**:102, 1889.

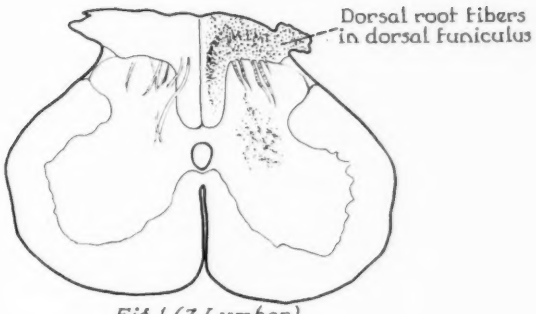

Fig. 1 (7 Lumbar)

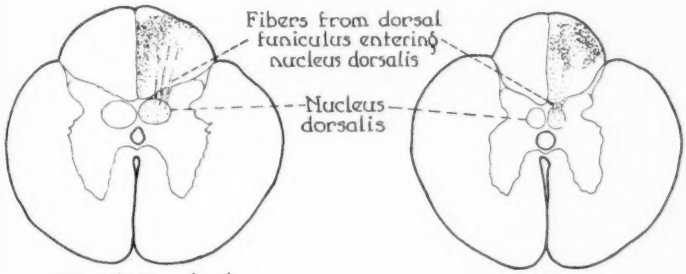

Fig. 2 (3 Lumbar)

Fig. 3 (1 Lumbar)

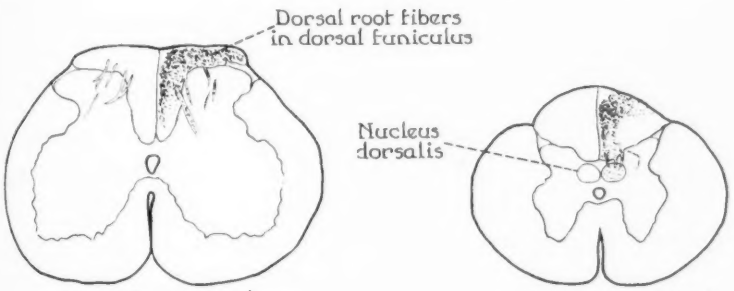

Fig. 4 (7 Lumbar)

Fig. 5 (2 Lumbar)

Fig. 1 (cat 89).—Transverse section of the seventh lumbar segment of the cord just above the level of the severed dorsal roots. This section shows degenerated fibers of the dorsal roots in the dorsal column and many degenerated fibers swinging into the gray matter.

Fig. 2 (cat 89).—Third lumbar level of the spinal cord of the same cat. This section shows fine degenerated fibers swinging into the nucleus dorsalis of the side operated on. Note the degeneration within the nucleus.

Fig. 3 (cat 89).—First lumbar level of the same cat. This demonstrates essentially the same facts as the previous section. This is the highest level in which degeneration could be demonstrated in the nucleus dorsalis in this animal.

Fig. 4 (cat 85).—Transverse section of the spinal cord at the seventh lumbar level, one segment above the highest dorsal root severed.

Fig. 5 (cat 85).—Second lumbar level of the cord of the same animal as in figure 4, showing as in cat 89, degenerated fibers entering the nucleus dorsalis from the dorsal funiculus. Note again the fine degeneration throughout the nucleus of the side operated on.

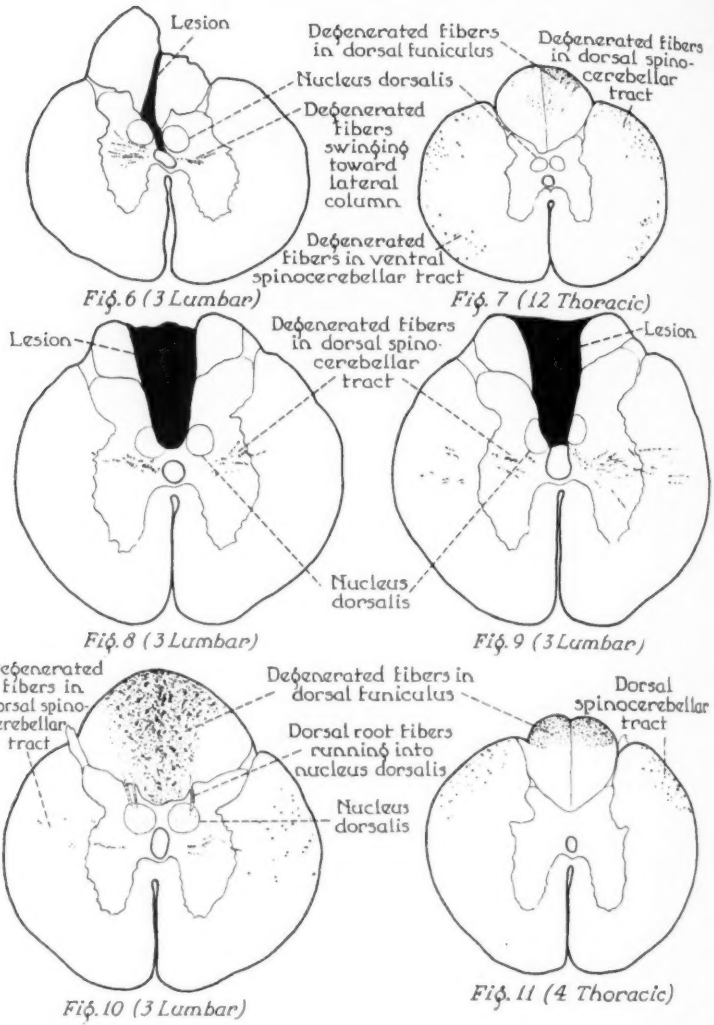

Fig. 6 (cat 83).—Transverse section of the spinal cord at the third lumbar level. The lesion passes between the two nuclei without destroying any part of either. Note the degenerated fibers on both sides streaming lateralward. These fibers must come from gray matter on the opposite side of the cord.

Fig. 7 (cat 83).—Twelfth thoracic level of the cord. This section shows equal numbers of degenerated fibers on each side in both the dorsal and the ventral spinocerebellar tracts.

Fig. 8 (cat 97).—Transverse section of spinal cord at the third lumbar level. The lesion has destroyed the medial portion of each nucleus dorsalis. This section represents the average extent of the lesion in this animal.

Fig. 9 (cat 97).—Transverse section of cord at the third lumbar level. This section shows the greatest extent of the lesion. In this section the dorsal gray commissure is interrupted; the total longitudinal extent of the interruption is, however, negligible.

Fig. 10 (cat 97).—Transverse section of the spinal cord of the same animal at the third lumbar level, above the lesion. Note again, as in cats 85 and 89, degenerated fibers swinging into Clarke's column on both sides, as well as degeneration within the nuclei themselves. Note also the degenerated fibers in the dorsal spinocerebellar tracts.

Fig. 11 (cat 97).—Fourth thoracic level of the cord of the same animal. This section shows degeneration in the dorsal spinocerebellar tracts alone, indicating that these tracts and these alone arise from the cells of Clarke's column.

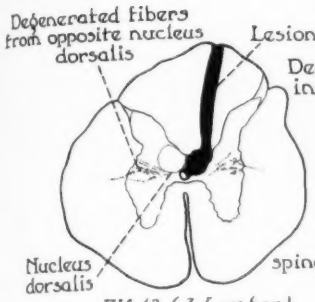

Fig. 12 (3 Lumbar)

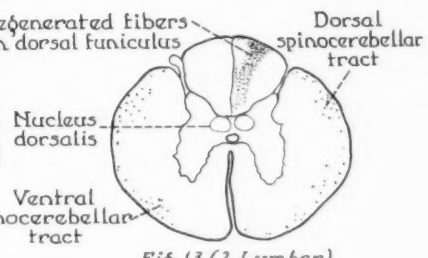

Fig. 13 (2 Lumbar)

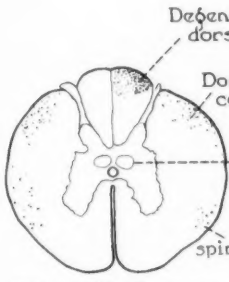

Fig. 14 (8 Thoracic)

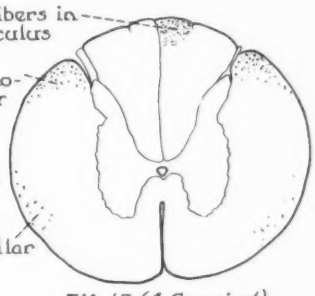

Fig. 15 (4 Cervical)

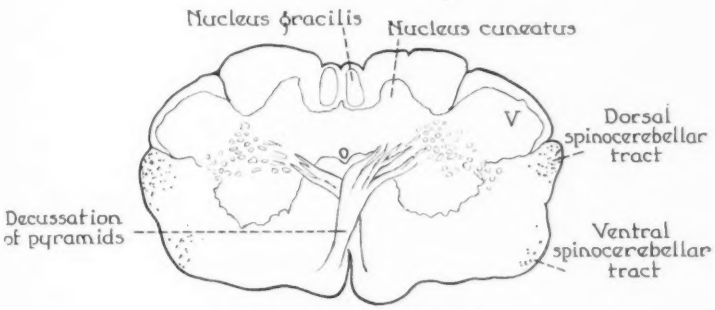

Fig. 16 (Lower medulla)

Fig. 12 (cat 93).—Transverse section of the spinal cord at the third lumbar level. The lesion (solid black) has destroyed the nucleus dorsalis of one side without injuring any adjoining gray matter. Note the degenerated fibers swinging toward the lateral columns in nearly equal numbers.

Fig. 13 (cat 93).—Transverse section of the second lumbar level above the lesion. Degenerated fibers are present in both the dorsal and the ventral spinocerebellar tracts of each side. The numbers of degenerated fibers on the two sides are practically equal.

Fig. 14 (cat 93).—Eighth thoracic level of the cord. Note the manner in which the spinocerebellar tracts tend to become concentrated as they pass toward the periphery of the cord.

Fig. 15 (cat 93).—Fourth cervical level of the spinal cord. Note especially the characteristic "inverted dipper" formation that the dorsal spinocerebellar fibers tend to assume (Beck [42]).

Fig. 16 (cat 93).—Transverse section of the brain stem through the lower medulla. Note the position of the spinocerebellar tracts.

the eleventh thoracic nerve was cut between the ganglion of the dorsal root and the cord. Marchi preparations of the cord of this animal showed degenerated fibers swinging from the posterior column into the gray matter; but, as is shown in figure 26, the main bundles of fibers appeared to swing past the column to end in nuclei adjoining it. It seems that if visceral rami end in Clarke's column it should be possible to trace well marked bundles of fibers into the column at the level of the eleventh thoracic segment, which corresponds with the influx of sensory fibers carried by the lesser splanchnic nerve. On the contrary, only as many fibers were found entering Clarke's column as might reasonably be expected to represent the unconscious proprioceptive fibers of the segmental body musculature. Practically identical results were obtained by sectioning the dorsal roots of the left thirteenth thoracic nerve in cat 92.

Despite the evidence presented in favor of the view that Clarke's column is a proprioceptive center, many have been hesitant about accepting this view because they knew of no corresponding nucleus for the upper extremity. For example, Freeman [49] stated: "The proprioceptive system as expressed in the spinal cord by the column of Clarke has not been accounted for in the brain stem."

In an attempt to find a nucleus for the upper extremity corresponding to Clarke's column, the dorsal roots of the seventh cervical nerve (in cat 100) and of the sixth cervical nerve (in cat 101) were cut. Marchi preparations in both experiments showed degenerated fibers ascending in the posterior column to the nucleus cuneatus. Both also showed the usual descending degeneration, which was confined to the comma tract of Schultze and which could be traced approximately for four segmental levels. In both cases, however, the degeneration had completely disappeared at the third thoracic segment, at which level Clarke's column first appears as a distinct nucleus in the cat (figs. 23 to 25). This indicates that no fibers from the brachial plexus are related to Clarke's column.

2. Cells in the Nucleus Cuneatus Homologous to Those in Clarke's Column.—Where, then, is the nucleus for the upper extremity homologous to Clarke's column? In studying Nissl preparations of the human brain stem one is at once struck by the similarity of the cells of Monakow's nucleus with those of Clarke's column. Morphologically, the cells of Clarke's column are so characteristic that the similarity is unmistakable. After a close comparison of the two nuclei, I thought that they represented part of the same system. A survey of the literature revealed that this has been remarked by others. Hollis,[17] the first

49. Freeman, W.: The Columnar Arrangement of the Primary Afferent Centers in the Brain Stem of Man, J. Nerv. & Ment. Dis. **65**:1. 1927.

observer to describe accurately the cells of Clarke's column, was able to trace a few cells from the cervical cord to the point where they merged with the nucleus cuneatus.

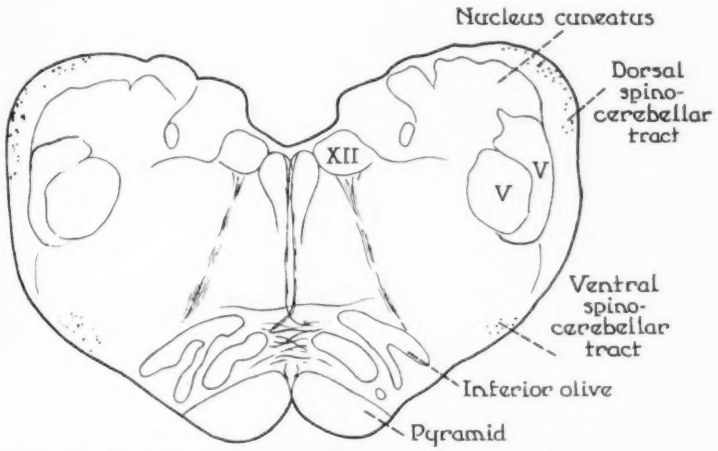

Fig. 17 Medulla oblongata through lower portion of IV ventricle

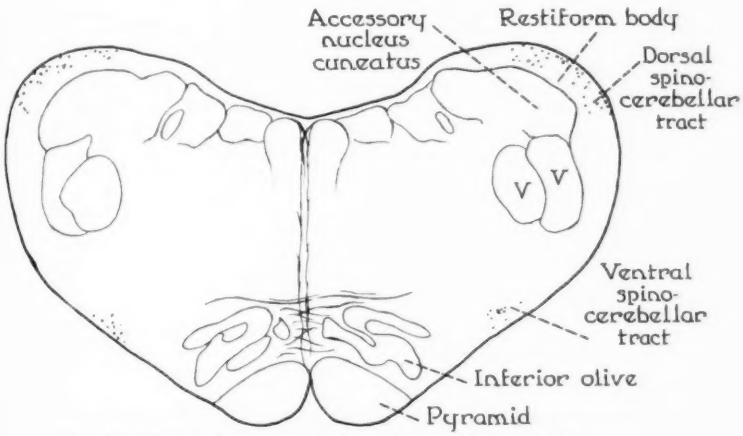

Fig. 18 Medulla oblongata through middle of inferior olive

Fig. 17 (cat 93).—Transverse section of the medulla oblongata through the lower portion of the fourth ventricle. The dorsal spinocerebellar tract is within the restiform body.

Fig. 18 (cat 93).—Transverse section of the medulla oblongata through the middle of the inferior olive. Note the positions of the spinocerebellar tracts. The nucleus labeled "accessory nucleus cuneatus" is Monakow's nucleus.

The nucleus cuneatus was first differentiated into inner and outer parts by Clarke,[1b] who remarked that the external portion of the nucleus

was characterized by the presence of larger and more variegated cells than are found in the internal portion. A more significant differentiation of the two parts of the nucleus cuneatus was made by von

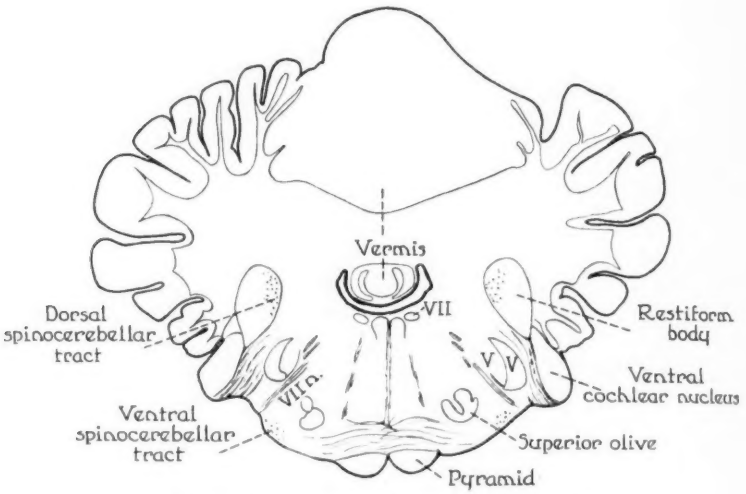

Fig. 19 Lower pons through superior olive

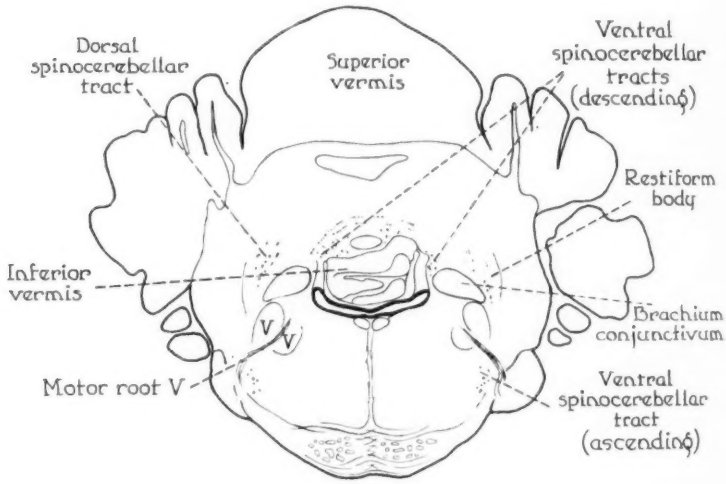

Fig. 20 Middle pons through exit of motor root of V nerve

Fig. 19 (cat 93).—Transverse section of the lower pons through the superior olive. Note the dorsal spinocerebellar tract within the restiform body.

Fig. 20 (cat 93).—Transverse section through the middle of the pons at the level of the exit of the motor root of the trigeminal nerve. The dorsal spinocerebellar tracts are swinging into the vermis of the cerebellum. In this section the descending loop of the ventral spinocerebellar tract is just posterior and medial to the brachium conjunctivum.

Monakow,[50a] who showed that, after injury of the pons in the region of the right inferior peduncle, secondary atrophy of the medial portion of the left cuneate nucleus was observed while the lateral portion

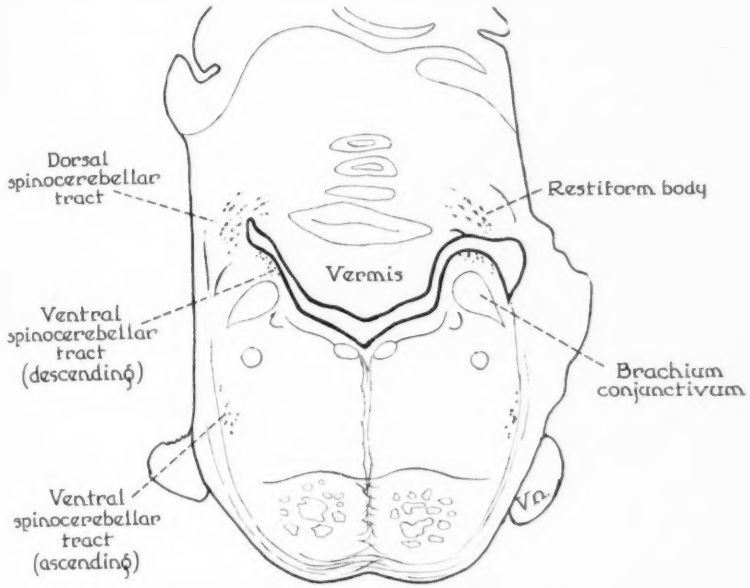

Fig. 21 Upper pons above V nucleus

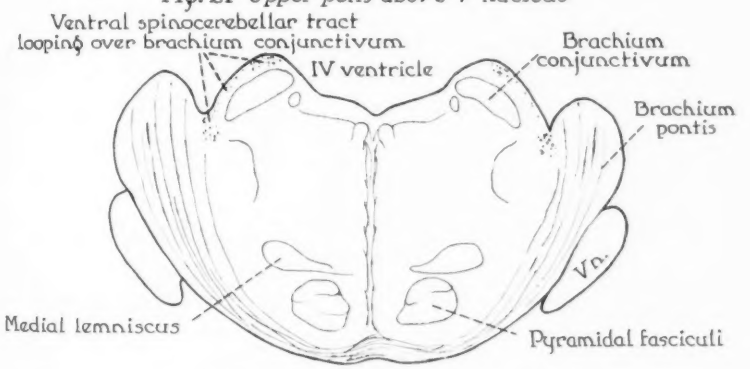

Fig. 22 Extreme upper border of pons

Fig. 21 (cat 93).—Transverse section of the upper pons above the nucleus of the trigeminal nerve. Note again the dorsal spinocerebellar fibers streaming into the vermis, and the two limbs of the ventral spinocerebellar tract.

Fig. 22 (cat 93).—Transverse section of the extreme upper end of the pons. Note the ventral spinocerebellar tract looping over the brachium conjunctivum to descend into the cerebellum.

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50. von Monakow, C.: (*a*) Neue experimentelle Beiträge zur Anatomie der Schleife, Neurol. Centralbl. **4**:265, 1885; (*b*) Striae acusticae und untere Schleife, Arch. f. Psychiat. **22**:1, 1891.

remained intact. Later, in 1891,[50b] he showed that when the right cerebellar hemisphere was injured atrophy of the right restiform body and of the lateral portion only of the cuneate nucleus resulted. These experimental observations are in accord with the finding by Menzel [51] of marked atrophy of the external parts of both cuneate nuclei in a case of hereditary ataxia in which both cerebellar hemispheres were

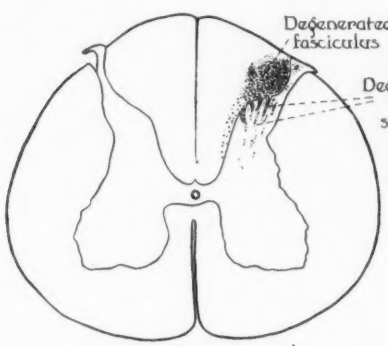

Fig. 23 (6 Cervical)

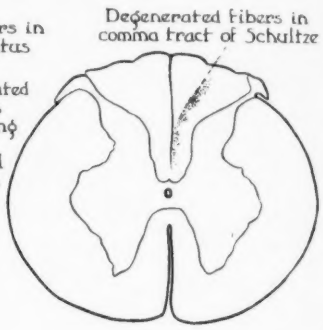

Fig. 24 (1 Thoracic)

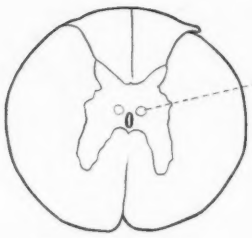

Fig. 25 (4 Thoracic)

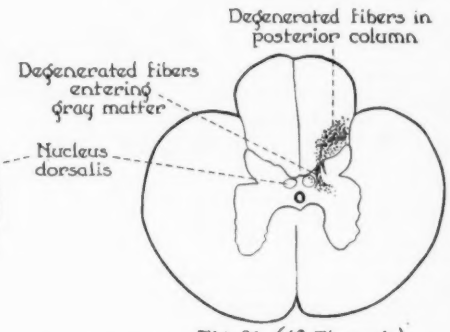

Fig. 26 (10 Thoracic)

Fig. 23 (cat 101).—Transverse section of the sixth cervical segment of the spinal cord. Note the degenerated fibers in the posterior column and the degenerated fibers swinging into the dorsal horn.

Fig. 24 (cat 101).—First thoracic level of the cord of the same animal. There are degenerated fibers in the comma tract of Schultze.

Fig. 25 (cat 101).—Fourth thoracic level of the spinal cord. Note the complete absence of degeneration in this section. Apparently the fibers of the dorsal roots of the brachial plexus do not descend to the upper end of Clarke's column.

Fig. 26 (cat 103).—Transverse section of the tenth thoracic level of the spinal cord, one segmental level above the dorsal root severed. Note the degenerated fibers of the dorsal roots in the posterior column. The degenerated fibers entering the gray matter sweep chiefly past the nucleus dorsalis (Clarke's column).

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51. Menzel, P.: Beitrag zur Kenntnis der hereditären Ataxie und Kleinhirnatropie, Arch. f. Psychiat. **22**:160, 1891.

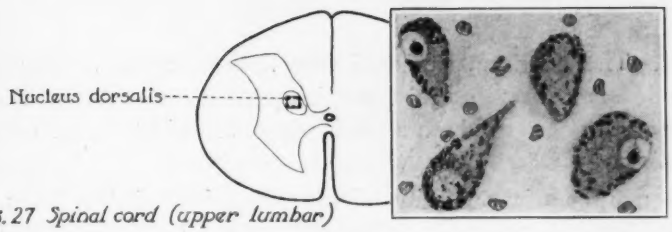

Fig. 27 Spinal cord (upper lumbar)

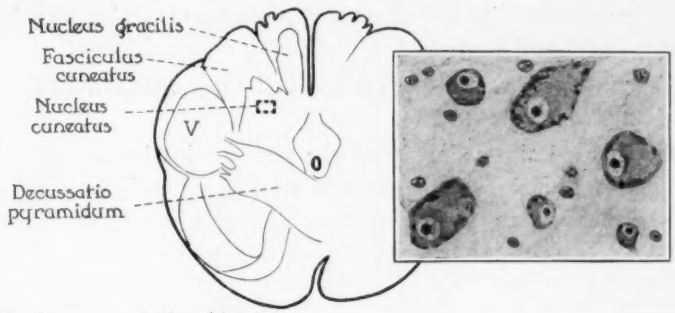

Fig. 28 Lower medulla oblongata

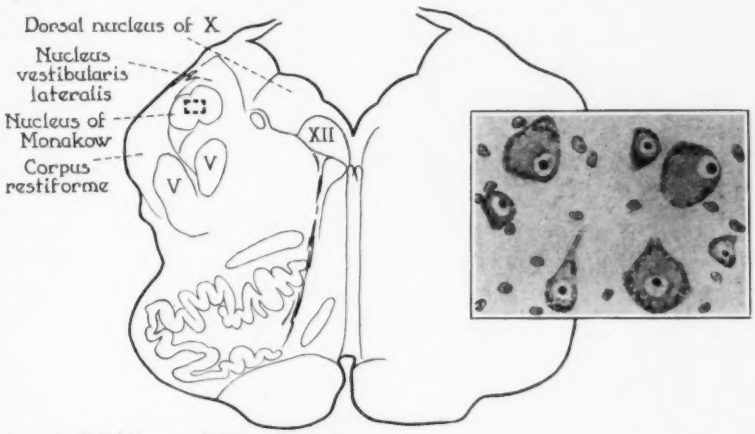

Fig. 29 Middle medulla oblongata

Fig. 27.—The human spinal cord in the upper lumbar region. The portion of the nucleus dorsalis within the rectangle is magnified and represented in detail at the right. Note the elongated character of the cells, their eccentric nuclei and the concentration of coarse Nissl granules at the periphery of the cells. The cells of the lumbar portion of the nucleus dorsalis are larger than those found elsewhere in the column (see Mott [31 d]).

Fig. 28.—The human medulla oblongata at the level of the pyramidal decussation. Field from the lower end of the nucleus cuneatus. Note the striking similarity in form and character of these cells to those represented above. These cells approximate in size those of the lower thoracic portion of the nucleus dorsalis.

Fig. 29.—The human medulla oblongata at the level of the middle of the inferior olive. Field from Monakow's nucleus (external nucleus cuneatus). Note again the similarity in size, shape and characteristics of these cells to those represented above.

atrophic. The inner cuneate nuclei were little affected. Similar observations demonstrating the functional independence of these portions of the cuneate nucleus have been made by other investigators, for example, by Flechsig and Hösel.[52]

The morphologic similarity of the cells of Clarke's column with those in Monakow's nucleus, as first pointed out by Hollis,[17a] was subsequently confirmed by Sherrington,[21] Blumenau [22] and others, including recently Gagel and Bodechtel.[23]

This similarity was also observed in human material in the present investigation (figs. 27 to 29).

Blumenau [22] also pointed out the analogy in the topographic relationships of Monakow's nucleus and of Clarke's column. It has been observed that in many cases Monakow's nucleus juts out from the posterior horn to extend into the white substance of the column of Burdach. There are, however, cases in which parts of Clarke's column are also separated and come to lie in the middle of the posterior column, as was first observed by Schultze.[53] In this regard, Sherrington [21] said: "The outlying cells in the funiculus cuneatus appear, in point of position, to hold the same relation to the inner mass of nucleus cuneatus as is held by the outlying cells in the external posterior column of the lumbothoracic cord to the vesicular column of Clarke." He concluded: "This seems to indicate that in the bulb the homologue of the vesicular column of Clarke is to be found in the cuneate nucleus."

Vegas,[54] Darkshevich and Freud,[55] Blumenau [22] and others have definitely demonstrated that Monakow's nucleus supplies many fibers directly to the restiform body of the same side. Blumenau concluded that "in view of the special relationships of the external cuneate nucleus to the restiform body, the analogies with Clarke's column of the spinal cord gain a further, physiologic significance. For as Clarke's column mediates the connection of certain fibers of the posterior column with Flechsig's tract, so the external cuneate nucleus stands in direct relationship to the posterior column on the one hand and to the central portion of the restiform body on the other."

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52. Flechsig, P., and Hösel, O.: Die Centralwindungen ein Centralorgan der Hinterstränge, Neurol. Centralbl. **9**:417, 1890.

53. Schultze, F.: Befund bei spinaler Kinderlähmung nach dreijährigem Bestehen derselben, Neurol. Centralbl. **1**:433, 1882.

54. Vegas, P.: Experimentelle Beiträge zur Kenntnis der Verbindungsbahnen des Kleinhirns und des Verlaufs der Funiculi graciles und cuneati, Arch. f. Psychiat. **16**:200, 1895.

55. Darkshevich, L., and Freud, S.: Ueber die Beziehung des Strickkörpers zum Hinterstrang und Hinterstrangskern nebst Bemerkungen über zwei Felder der Oblongata, Neurol. Centralbl. **5**:121, 1886.

Since the nucleus of Monakow receives from the funiculus cuneatus fibers which are a continuation of the cervical and superior thoracic dorsal roots, one must consider this nucleus an important relay station between peripheral stimuli which come from the arm, the neck and the upper part of the trunk, on the one side, and from the cerebellar cortex on the other. Hence Monakow's nucleus probably plays the same part in relation to the cervical and upper thoracic dorsal roots that the column of Clarke does in relation to the lower thoracic, lumbar and sacral dorsal roots.

3. *Proportion of Crossed to Uncrossed Fibers in the Dorsal Spino-Cerebellar Tract.*—Considerable attention was paid to the question of the amount of crossing of the dorsal spinocerebellar tracts. After many attempts, I finally succeeded, in cat 93, in destroying the left nucleus dorsalis for a distance of 1.4 mm. without apparent injury to the nucleus of the opposite side or to any contiguous gray matter. Marchi preparations of the site of this lesion showed bundles of degenerated fibers swinging toward each lateral column in approximately equal numbers (fig. 12). Inspection of the sections above the level of the lesion revealed nearly equal numbers of degenerated fibers in each dorsal spinocerebellar tract (figs. 13 to 16). Since no part of the nucleus of the right side was injured, one might conclude that about half the fibers are direct and half are crossed. But a close study showed that the majority of fibers arising from Clarke's column cross to the opposite side in their ascent. The lesion destroyed the nucleus of one side and interrupted the fibers coming from the nucleus of the opposite side. It was possible to verify this in cat 83, in which the capillary pipet passed between the two columns without apparently destroying an appreciable part of either. Marchi preparations of the cord of this animal showed an abundance of degenerated fibers swinging toward the lateral columns (fig. 6). Segments above the lesion in this cat (83, fig. 7) showed degenerated fibers practically equal in number to those obtained in cat 93, in which a corresponding length of Clarke's column was completely destroyed (figs. 12 and 13). This would seem to warrant the conclusion that practically all the fibers arising from Clarke's column in the cat cross in their ascent.

An attempt was made to produce retrograde chromatolysis and cell atrophy in Clarke's column by cauterizing the left dorsal spinocerebellar tract at the ninth thoracic level (cat 102) and thus to check the former result by other technic. The Nissl technic was applied to the cord after the animal had survived for four weeks. The results obtained were suggestive, but unfortunately not sufficiently conclusive to warrant further discussion. The time allowed was either too long for typical chromatolysis or too short for atrophy to occur. The peculiar distribution of coarse granules of Nissl substance about the periphery and

the attenuated condition of the chromatic substance in the interior of the cell render a study of this kind more than usually difficult.

4. *Relation of the Nucleus Dorsalis to the Ventral Spinocerebellar Tract.*—In the course of experiments 83 and 93 there appeared degenerated fibers also in the ventral spinocerebellar tracts of both sides, indicating that possibly the ventral spinocerebellar tracts also arise from the cells of Clarke's column (figs. 6 and 7 and 13 to 16). There is abundant authority favoring such a conclusion (Pellizi,[39] Schäfer,[32] Lewandowsky,[33] Marburg,[34] Schäfer and Bruce,[35] Obersteiner[38] and others). However, careful examination of both lesions showed that they penetrated to the central canal, interrupting all the fibers passing through the dorsal gray commissure. The significance of this fact became apparent when cat 97 was examined. In this animal, in spite of the fact that the lesion destroyed the medial portions of both nuclei dorsalis, it reached only an insignificantly minute segment of the central canal (figs. 8 and 9), and there was no ascending degeneration in the ventral spinocerebellar tracts. This suggests that the nucleus dorsalis does not give origin to fibers of the ventral spinocerebellar tract in the cat (figs. 10 and 11). Apparently, in the cat at least part of the fibers of the ventral spinocerebellar tract cross in the dorsal gray commissure.

The ventral spinocerebellar tract evidently is not homologous to the dorsal spinocerebellar tract. It is probable that it may prove to be part of the long-sought visceral sensory system of the spinal cord, as is indicated by the experiments of Spiegel and Bernis,[56] who found that only after bilateral destruction of the ventral spinocerebellar tracts alone did stimulation of the splanchnic nerves fail to produce inhibition of respiration.

In the course of these experiments it was possible to trace both spinocerebellar tracts to their termination in the cerebellum and to verify the direct entrance of the dorsal spinocerebellar tract via the restiform body and the looping of the ventral spinocerebellar tract over the brachium conjunctivum in its descent into the cerebellum (figs. 13 to 22). These points have been so recently studied (Beck[42]) that no detailed comments are necessary at this point.

SUMMARY

1. Section of the sacral and lower lumbar dorsal roots of the cat resulted in degeneration of the fibers ending in and about Clarke's column as high as six segmental levels above the highest dorsal root severed.

56. Spiegel, E. A., and Bernis, W. J.: Beiträge zum Studium des vegetativen Nervensystems: IX. Mitteilung; Die Rückenmarksbahn der Visceralsensibilität, Arch. f. d. ges. Physiol. **210**:209, 1925.

2. Section of the dorsal roots of the midthoracic nerves resulted in degenerated bundles of fibers swinging chiefly past Clarke's column to end in the adjoining gray matter. Only as many fibers were found entering Clarke's column as might be expected to subserve the unconscious proprioceptive functions of the segmental body musculature.

3. The morphologic similarity of the cells in Clarke's column to those in Monakow's nucleus magnocellularis (external nucleus cuneatus), the analogous topographic position of the two nuclei and the fact that Monakow's nucleus supplies the restiform body with a special bundle of fibers probably analogous to the dorsal spinocerebellar tract indicate that Monakow's nucleus probably plays the same rôle in relation to the cervical and upper thoracic dorsal roots that Clarke's column does to the lower thoracic, lumbar and sacral roots.

4. Experimental destruction of one nucleus dorsalis and lesions between the two nuclei demonstrated that in the cat practically all the fibers arising from the nucleus of one side cross to ascend in the dorsal spinocerebellar tract (Flechsig's) of the opposite side.

5. Attempts to confirm this crossing by the discovery of retrograde chromatolysis and atrophy of cells in Clarke's column of one side as a result of cauterizing the dorsal spinocerebellar tract of the opposite side were suggestive but inconclusive.

6. Lesions restricted to Clarke's column resulted in degeneration in the dorsal spinocerebellar tract alone, indicating that in the cat the nucleus dorsalis does not contribute fibers to the ventral spinocerebellar tract (Gowers').

7. The ventral spinocerebellar tract in the cat crosses in part, at least, in the dorsal gray commissure.

8. The conventional representation of the course of both spinocerebellar tracts in the cord and brain stem and their mode of termination in the cerebellum are confirmed.

CHANGES IN THE BRAIN IN LEGAL ELECTROCUTION

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As in cases of fatalities that are caused by lightning or by contact with powerful industrial currents, death in so-called legal electrocution is caused by an electric shock. Whereas the extent and the nature of accidental electric injuries to various organs—the skin, muscles and heart—have been repeatedly studied, histopathologic investigations of the central nervous system in cases of legal electrocution are scarce. Such studies may even seem superfluous, for the etiologic factor is the same in all forms of death by electricity. Yet differences in the histologic changes in the nerves may be expected. For instance, in legal electrocution the current always enters the cranial cavity and traverses the entire central nervous system; the strength of the current is known; its action is more prolonged than that in accidental electrocution, and death is practically instantaneous. As the general physical condition of a condemned subject is good, his central nervous system is not liable to become affected by a prolonged physical ailment or the agonal stage of a disease. Necropsy is performed almost immediately, and for this reason the brain is especially suitable for histologic studies.

The conditions are different in accidental electrocution. The electric current enters the body at any point—the hand, foot or neck; because of imperfect contact, the exact amount of electricity that passes through the body is usually not known; death may occur hours, days or even months after the accident, regardless of the strength of the current that was used. For the foregoing reasons, the general health of the victim may become impaired; a protracted ailment may develop, and in case of death necropsy may be delayed for hours or even days. In the case of Mott and Schuster,[1] for instance, it was performed thirty-nine hours after death. Such cases are much less favorable for histopathologic observations than those of legal electrocution.

From the Laboratory of Neuropathology of the University of Illinois College of Medicine.

Read at the Fifty-Ninth Annual Meeting of the American Neurological Association, Washington, D. C., May 10, 1933.

1. Mott, F. W., and Schuster, E.: Proc. Roy. Soc. Med. (Path. Sect.) **3**:140, 1909-1910.

Through the kindness of Dr. Paul Schroeder, State Criminologist, and the cooperation of Dr. George Milles of the department of pathology of the University of Illinois, College of Medicine, I was able to study the brains of five criminals who had been electrocuted at the Southern Illinois Penitentiary.

MATERIAL

The ages of the subjects ranged between 24 and 58 years; the alternating current which was used was passed from the forehead to the feet in four shocks. The strength of the first and third shocks was 2,300 volts, and each lasted seven seconds; the strength of the second and fourth shocks was 550 volts, and the duration was fifty-two seconds.

Necropsies were performed immediately, and the brains were placed at once in various fixation fluids. Three brains were fixed in a 10 per cent solution of formaldehyde; one brain was placed in toto in a 96 per cent solution of alcohol, and one was fixed in Zenker's fluid. The brain which was fixed in alcohol was especially valuable, as alcohol-fixed nerve tissues stain especially well with toluidine blue, thionine and similar substances, and permit compliance with the rules laid down by Nissl for the study of the histologic changes in the ganglion cells. However, the staining qualities of this brain tissue differed in no way from those presented by the formaldehyde-fixed brain tissues, which could be studied also in frozen sections with additional methods and therefore more thoroughly.

Macroscopic Observations.—No macroscopic changes, such as manifest hemorrhages or softening, were detected in the meninges, gray or white substance, ventricles, choroid plexus or the basilar blood vessels of the brain.

Microscopic Observations.—The architecture of the cortex showed no changes. The demarcation between the gray and white substances was distinct. The subpial layer or lamina zonalis was more areolar than normal; it was considerably rarefied. In some instances, this layer was separated, as if torn from the superimposed pia, and the margins of the separated layers appeared ragged and shaggy (fig. 1). In the cerebellum the loose contact between the cortical layers was often in evidence between the molecular layer and that of the Purkinje cells (fig. 2). Some areas of the brain tissues were thin, pale and areolar. They often exhibited small rents, tears or cracks, or appeared as narrow slits which were sometimes filled with fragments of brain tissue. In other areas the defects occurred as fissurations (fig. 3), and easily impressed one as artefacts such as are sometimes present in frozen sections or in brains which had been poorly handled and improperly fixed. Brains that are fresh, well fixed, obtained from relatively healthy subjects and embedded in celloidin do not exhibit defects in the form of fissurations, cracks or fragmentation. When such defects are present under the aforementioned circumstances of hardening and embedding, they are to be looked on as pathologic.

Cellular Changes: The most common type of cellular change was that of swelling (figs. 4 and 5). Swollen ganglion cells were present in every layer of the cortex. Such cells usually appeared well stained; the processes were tortuous and also well stained and, like the cell body, showed the presence of chromophilic granules. In the deeper layers of the cortex many ganglion cells presented marked phenomena of satellitosis and neuronophagia (fig. 6). Some ganglion cells were dislocated (fig. 7); others appeared as though eaten away, excavated or invaded by neuronophages. Other ganglion cells were vacuolated, torn up and homogeneous, and some cells were liquefied (fig. 8). In the liquefied ganglion cells, the cell

body and the processes appeared alike—pale, somewhat granular and devoid of chromophilic substance. The nucleus possessed an indistinct membrane and was often misshapen, excavated or oblong; in some instances it was broken up and contained a few chromatin granules, which were barely discernible (karyolysis). No changes were detected in the neurofibrils, which could distinctly be discerned, especially in the cell processes. In specimens that were stained according to the method of Alzheimer-Mann, the processes appeared as pale streaks crossing the visual field (fig. 9). On the whole, however, the changes in the nerve fibers were not so striking or so variable as those in the ganglion cells. The changes in the latter varied from plain swelling to complete chromatolysis and neuronophagia and, in general, were analogous to the changes which have been thoroughly described by Corrado [2] in experimental animals.

Fig. 1.—Rents in the subpial layer of the cortex, which is torn off the pia (*P*). Toluidine blue stain (fixation in formaldehyde); reduced from a magnification of × 490.

Though some cellular changes, for instance, vacuolation (Fish [3]) and swelling, were common, they were not striking enough to attract attention, and for this reason could easily be overlooked. On the other hand, changes which were striking, such as liquefaction and fragmentation of the ganglion cells, were rare.

The changes were not confined to particular areas, such as the medulla or the olivary bodies. They were universal and were probably more marked in the cortex than in the brain stem, but were especially in evidence along the cracks or the fissures. In the spinal cord, which could be studied only in the upper cervical region, the cellular changes were milder. They appeared as slight swelling and occasional neuronophagia. The nerve fibers were usually normal. In many

2. Corrado, G.: Di alcune alterazioni della cellula nervosa nella morte per elettricità, Atti d. r. Accad. med.-chir. di Napoli **52**:242, 1899.

3. Fish, P. A.: The Action of Strong Currents of Electricity upon Nerve Cells, Tr. Am. Micr. Soc. **17**:180, 1895.

instances the myelin was swollen and, as I have pointed out, appeared in specimens stained according to the method of Alzheimer-Mann as white stripes crossing the visual field (fig. 9). No evident changes were present in the axons.

Glia: In the subpial layer the glia nuclei exhibited a distinct supply of cytoplasm, which was often granular as though broken up. In the white substance the glia nuclei often formed clusters or rosettes. A common occurrence was so-called acute swelling of oligodendroglia, in which a glia nucleus, usually rich in chromatin, was surrounded by an empty space bridged by threads connecting the nucleus with the surrounding parenchyma. In many instances the abundant chromatin content of

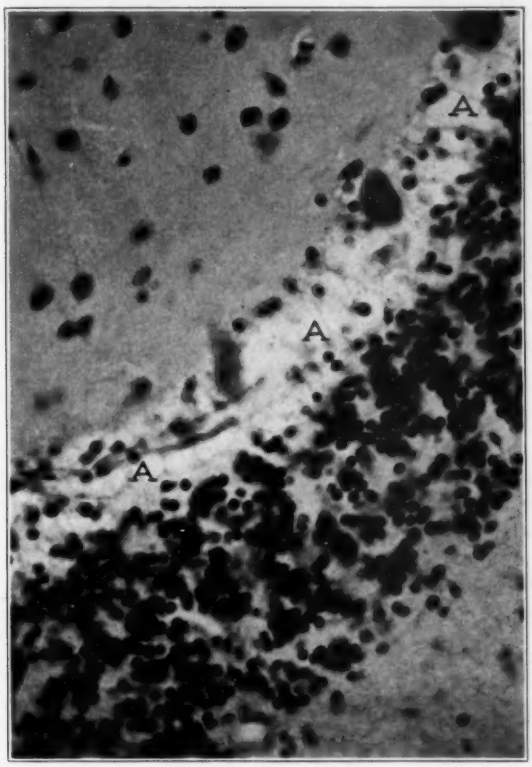

Fig. 2.—The cerebellum; the granular layer is divided from the layer of Purkinje cells by a thinned and fenestrated area (*A, A, A*). Toluidine blue stain (fixation in formaldehyde); reduced from a magnification of × 490.

the nucleus was reduced to a few granules and the nucleus was rendered indistinct (karyolysis). In the subependymal area of the medulla glia cells were especially numerous; many of them were rich in cytoplasm.

Mesodermal Changes: The blood vessels were often congested and frequently exhibited so-called shrinkage spaces (spaces of His). The spaces of His were unusually wide and appeared as broad collars traversed, as in the swollen oligodendroglia, by bands of glia fibers (fig. 5). Hemorrhages were rare; when present, they were confined to the adventitial or perivascular spaces, while petechial hemorrhages were absent. In the large blood vessels, the basilar artery, for

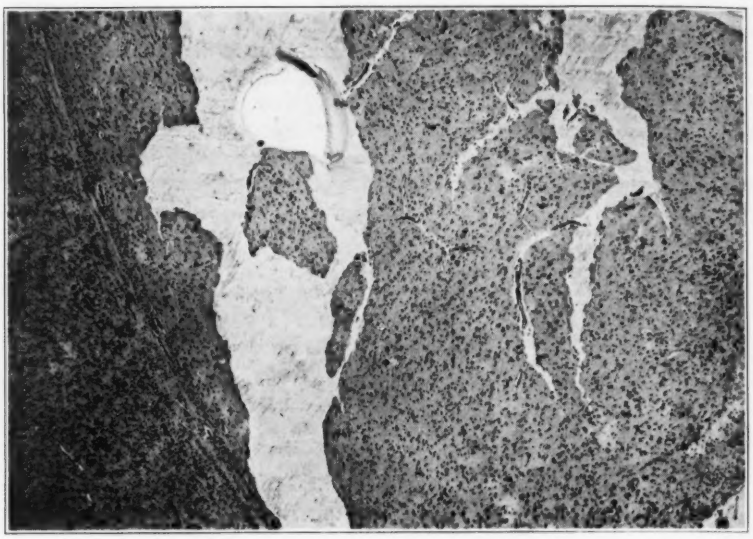

Fig. 3.—Fissuration (large defects) and slits (minor defects) in the cortex of the brain. Toluidine blue stain (fixation in alcohol); reduced from a magnification of × 550.

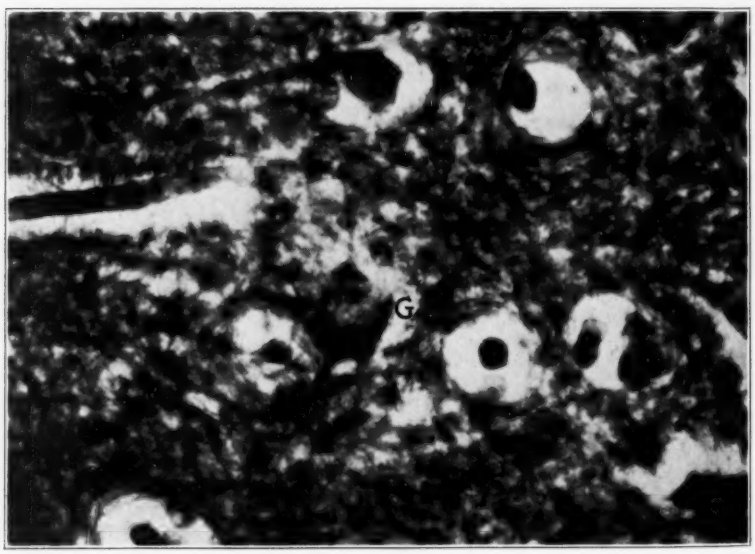

Fig. 4.—A large, swollen ganglion cell (*G*) with distinct processes containing well stained and unaffected fibrils. The glia nuclei are surrounded by large spaces of shrinkage described as acute swelling of the oligodendroglia. Bielschowsky stain; reduced from a magnification of × 1,200.

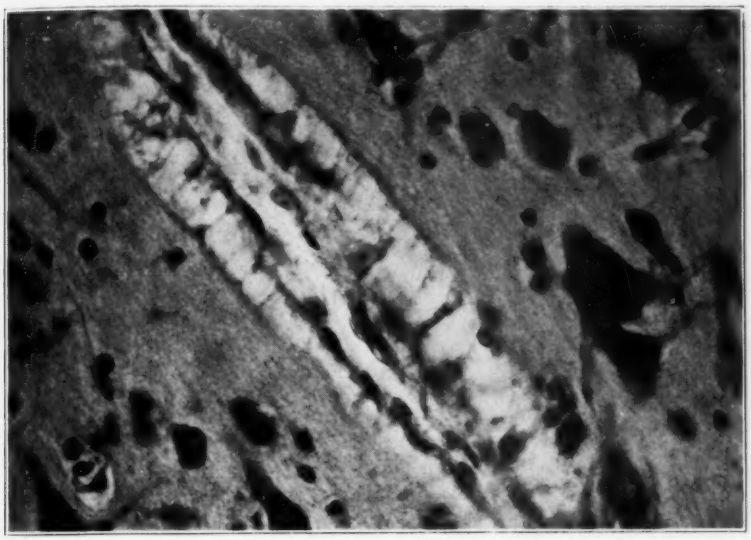

Fig. 5.—Rarefaction and distention of the periadventitial areas (shrinkage spaces or spaces of His) traversed by bridges of glial fibers. To the right is a swollen ganglion cell in which chromophil or Nissl granules can be discerned. Toluidine blue stain (fixation in formaldehyde); reduced from a magnification of × 620.

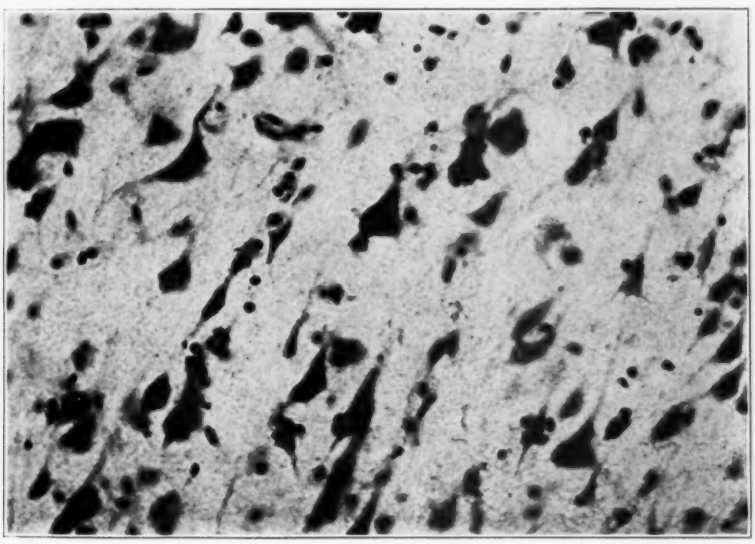

Fig. 6.—The phenomena of neuronophagia and satellitosis in the lower cortical layers. Toluidine blue stain (fixation in alcohol); reduced from a magnification of × 450.

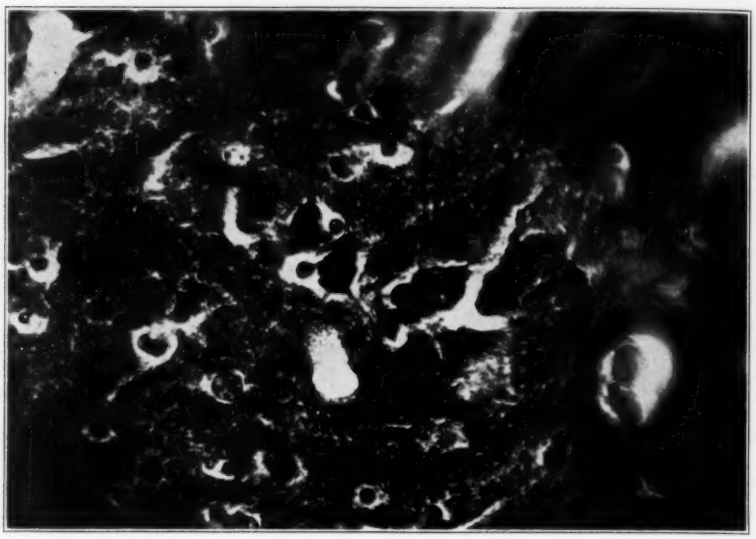

Fig. 7.—In the center is a group of ganglion cells. The cell to the right exhibits a swollen axon; the two ganglion cells to the left of this cell appear dislocated; the periganglionic spaces are distended (from shrinkage of the surrounding parenchyma). Bielschowsky stain; reduced from a magnification of × 670.

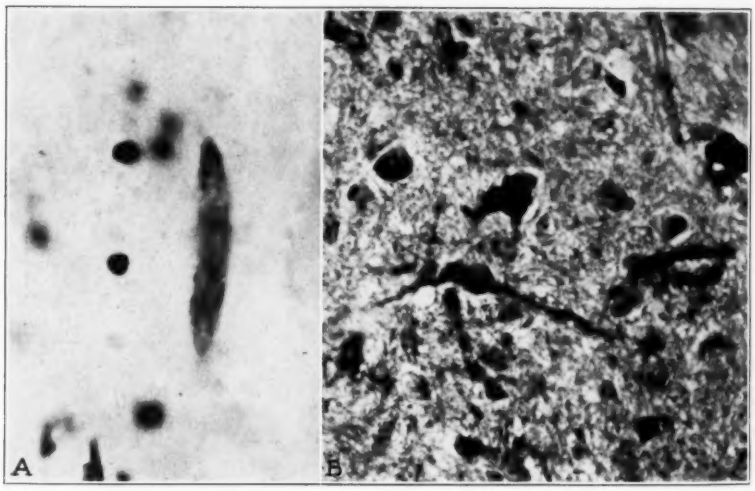

Fig. 8.—*A*, an elongated, homogeneous and granular ganglion cell. Toluidine blue stain; reduced from a magnification of × 1,100. *B*, some tumified ganglion cells; their processes, like the cell bodies, are homogeneous, tortuous and swollen. Alzheimer-Mann stain; reduced from a magnification of × 490.

Fig. 9.—The field is traversed by white stripes as if by demyelinated cortical nerve fibers. Alzheimer-Mann stain; reduced from a magnification of × 330.

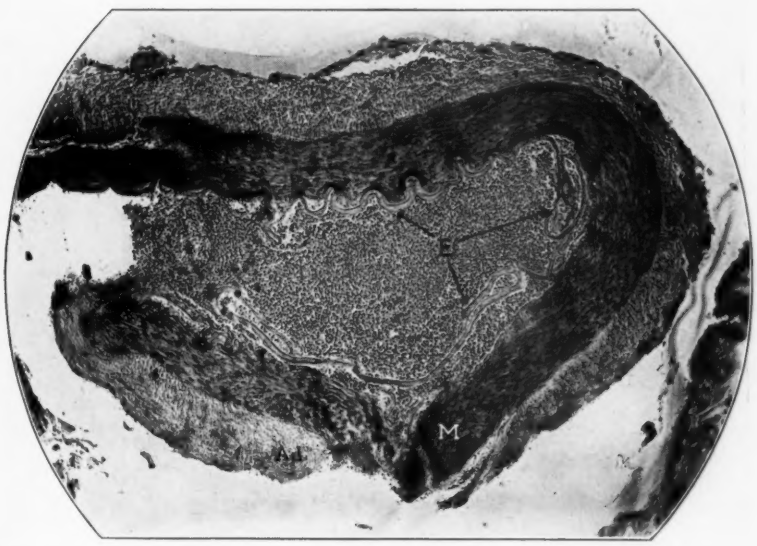

Fig. 10.—A damaged basilar artery in a subject, aged 31. *E*, the elastic membrane (to the right it is torn, appearing as loops); *M*, muscularis, divided almost in two; *Ad*, a torn adventitia. The tissue was fixed in Zenker's fluid; reduced from a magnification of × 78.

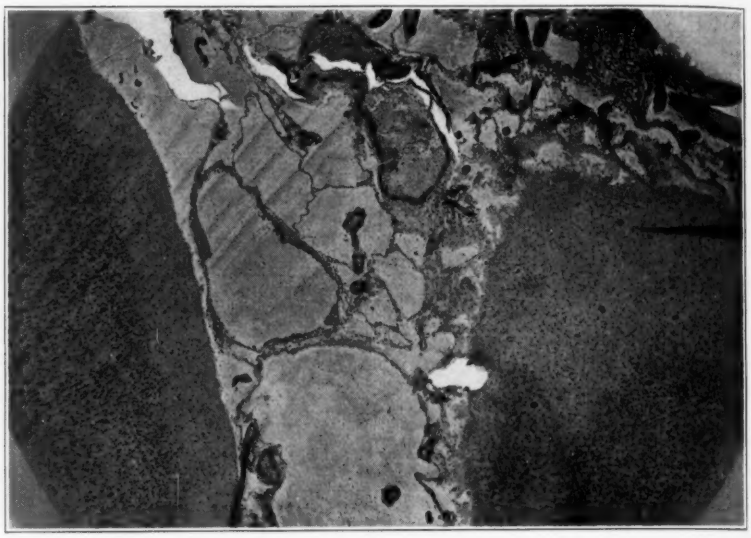

Fig. 11.—The meshes of the subarachnoid spaces are distended and the trabeculae are cellular. Toluidine blue stain; reduced from a magnification of × 34.

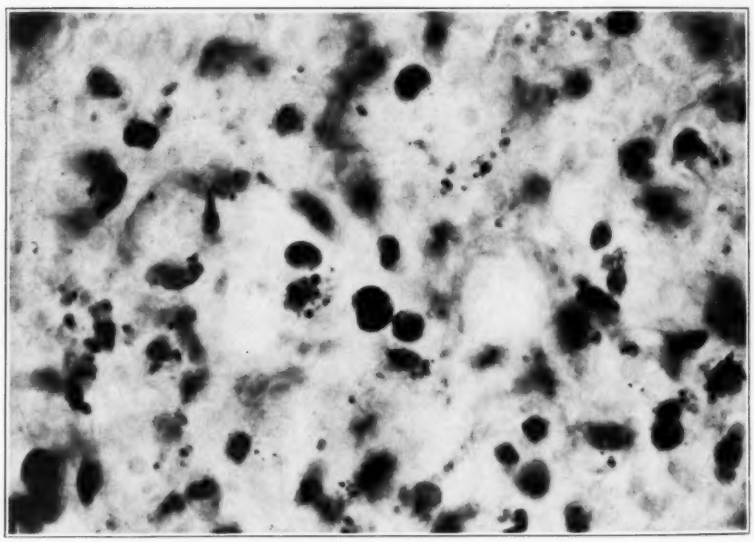

Fig. 12.—The types of cells in the subarachnoid space described in the text. Toluidine blue stain (fixation in Zenker's fluid); reduced from a magnification of × 950.

instance, the walls were in some cases ruptured (fig. 10), as if divided by a blunt instrument, or the elastica alone was separated from the rest of the wall; it was broken up in fragments which lay curled within the vascular lumen (fig. 10). In other cases the vascular wall was merely thinned, and the adventitia, which was the only tunic unaffected, protruded in the form of an aneurysm. The vascular changes here mentioned were not present in the small blood vessels, which, as noted, were merely congested.

The pia was widely separated from the arachnoid membrane, and the subarachnoid space appeared as a conglomeration of widened meshes (fig. 11). The latter were, for the most part, empty. In some places they were obliterated by masses of cells, the majority of which were mesothelial. They stained unusually well and often appeared flattened or concave as if plastered on the trabeculae of the subarachnoid space. Other mesothelial cells formed clusters and were intermingled with polyblasts which appeared as pale, horseshoe-shaped nuclei and contained only a few granules of chromatin. In one brain the cellular contents of the meshes were unusually numerous (fig. 12) and consisted of lymphocytes, polyblasts and even gitter cells. Hemorrhages were rare and were occasionally present around the pons and in the region of the peduncles.

No striking changes were found in the pacchionian bodies or the dura, but changes were quite evident in the choroid plexus. The tuft cells were distended and areolar, and the stroma was covered with numerous cell bodies, lymphocytes, polyblasts and gitter cells.

Summary.—The changes outlined were present in each of the five brains and pertained to the ganglion cells, glia, blood vessels and pia-arachnoid. They may be summed up as: mild and severe cellular alteration, from swelling to liquefaction; distention of the subarachnoid space and of the spaces around the oligodendroglia and the blood vessels; rupture of the walls of the blood vessels, especially of the internal elastic membrane; shrinkage, thinning and breaking up of the cerebral parenchyma with the formation of rents or tears, slits or fissures, and extreme scarcity or complete absence, in the majority of cases, of hemorrhages in both the meninges and the cerebral parenchyma.

COMMENT

Of the foregoing changes the most outstanding are the tears of the parenchyma of the brain and of the blood vessel walls. Other changes resembled those described in experimental animals by Grange,[4] Capogrossi,[5] Corrado,[2] Urquhart[6] and, more extensively, by Langworthy and Kouwenhoven[7] and Morrison, Weeks and Cobb.[8] The changes emphasized by experimental workers were not the parenchy-

4. Grange, E.: Des accidents produits par l'électricité, Ann. d'hyg. **13**:53, 303, 1885.

5. Capogrossi, A.: Contribution à l'étude des caractères anatomo-pathologiques de la mort par l'électricité, Arch. internat. de méd. lég. **1**:236, 1910.

6. Urquhart, R. W. Ian: Experimental Electric Shock, J. Indust. Hyg. **9**:140, 1927.

7. Langworthy, O., and Kouwenhoven, W. B.: An Experimental Study of Abnormality Produced in the Organism by Electricity, J. Indust. Hyg. **12**:31, 1930.

8. Morrison, L. R.; Weeks, A., and Cobb, S.: Histopathology of Different Types of Electric Shock on Mammalian Brains, J. Indust. Hyg. **12**:324 and 364, 1930.

matous and vascular tears, but hemorrhages in the brain and pia, swelling and liquefaction of the ganglion cells in the deeper layers of the cortex, satellitosis and neuronophagia, shrinkage of cells, increase in the number of glia nuclei, and swelling of the oligodendroglia and of the myelin in cases in which death was immediate. In the cases in which the animals survived for weeks the evident changes were perivascular gliosis and degeneration of the nerve. It is interesting to note that in experimental electrocution marked hemorrhages were prevalent only when the alternating current was used and were inconspicuous with the direct electric current. In many observations (MacMahon [9]), the hemorrhages were petechial in the meninges of the brain and of the cord.

Changes similar to those observed in experimental animals were noted in accidental electrocution. In both, as pointed out by Jellinek,[10] Kawamura [11] and Karnosh,[12] the hemorrhages were the outstanding feature, though Langworthy and Kouwenhoven spoke in the report of their two cases (one was a case of accidental, the other of legal, electrocution) of only "small petechial hemorrhages in the brain stem."

In five legally electrocuted criminals, Spitzka and Radasch [13] described in the brains peculiar circular areas, from 25 to 300 microns in diameter, especially around the blood vessels. "They appeared as delicate, small meshed reticulum, especially in the interolivary white substance or around the olivary body, in the pons, corpora quadrigemina and mainly in the longitudinal tracts." In three cases these authors described a rugged appearance of some areas. Spitzka and Radasch ascribed the circular areas, which evidently corresponded with the shrinkage spaces of His, to a possible sudden liberation of bubbles of gas because of the "electrolytic properties of the current," as it seeks the paths of the least resistance along the vessels. R. Jaffé [14] and, later, Langworthy and Kouwenhoven saw the cause in an excessive formation of heat. However, neither liberation of bubbles of gas nor excessive formation of heat can explain the rents. Rents, for instance,

9. MacMahon, H. E.: Electric Shock, Am. J. Path. **5**:333, 1929.

10. Jellinek, S.: Histologische Veränderungen im menschlichen und thierischen Nervensystem, theils als Blitz—theils als elektrische Starkstrom-Wirkung, Virchows Arch. f. path. Anat. **170**:56, 1902; Die Eigenart der elektrischen Verletzung und ihre ärztliche Wertung, Wien. klin. Wchnschr. **31**:1173 and 1207, 1918.

11. Kawamura, I.: Elektropathologische Histologie, Virchows Arch. f. path. Anat. **231**:570, 1921.

12. Karnosh, L. J.: The Neurological Aspects of Industrial Electrocution, Ohio State M. J. **28**:786 (Nov.) 1932.

13. Spitzka, E. A., and Radasch, H. E.: The Brain Lesions Produced by Electricity as Observed After Legal Electrocution, Am. J. M. Sc. **144**:341, 1912.

14. Jaffé, R. H.: Electropathology: A Review of the Pathologic Changes Produced by Electric Currents, Arch. Path. **5**:837 (May) 1928.

have not been emphasized in cases of caisson disease in which bubbles of gas are also liberated, nor have they been observed in cases of sunstroke or heatstroke, though the temperature in legal electrocution may be much higher than that in heatstroke. Thus Spitzka [15] observed a temperature of from 120 to 129.5 F. within twenty minutes, and stated that after the removal of the brain, the temperature recorded in the vertebral canal was often 120 F. A still higher temperature (145 F.) was observed by Werner.[16] Notwithstanding such high temperatures, the overheated brain did not exhibit changes which are usually present in sunstroke or heatstroke. In my opinion, the changes observed in legal electrocution are due to purely mechanical factors. The action of a strong electric current is equivalent to a direct mechanical injury similar to that which the cerebral tissues sustain, for instance, in concussion of the brain or cord. As shown elsewhere,[17] in spinal concussion, owing to a momentary violent jarring, there occur minute scattered foci of degenerative softening. In legal electrocution, the mechanical factor—the jarring—is the electric current. It tears, as it were, the nerve fibers and breaks them up into small fragments, producing rents or cracks and thinning of the cerebral parenchyma with shrinkage around the blood vessels, beneath the pia or around the glia nuclei. The significance of the rents is the same as that of the thinning of the parenchyma or the shrinkage around the glia nuclei and the blood vessels and their tearing. It is a reaction to a strong electric current, the foregoing types of changes differing only in extent. Some suggestions to such a view may be found in the literature. Thus Spitzka and Radasch [13] spoke of a ragged appearance of some areas, as though the tissues "had been torn by some diffusely explosive or disruptive force." Occasionally they even saw ruptured myelin. Langworthy and Kouwenhoven [18] stated that "often longer cavities, entirely unrelated to blood vessels, were found in the cerebral hemispheres. In cases where the pathway of the current was from one foreleg to the tail, cavities were found in the spinal cord." Interesting and suggestive is the statement by the same authors that in some experimental cases "it was almost as if the cell had been blown to pieces by dynamite," and that the changes in the ganglion cells set in "with explosive suddeness and the electric current apparently reacts violently upon the constituents

15. Spitzka, E. A.: Observations Regarding the Infliction of the Death Penalty by Electricity, Proc. Am. Phil. Soc. **47**:39, 1908.

16. Werner, A. H.: Death by Electricity, New York M. J. **118**:498, 1923.

17. Hassin, G. B.: Concussion of the Spinal Cord: A Case with the Clinical Picture of Amyotrophic Lateral Sclerosis, Arch. Neurol. & Psychiat. **10**:194 (Aug.) 1923.

18. Langworthy, O., and Kouwenhoven, W. B.: Injuries Produced by Contact with Electric Circuits, Am. J. Hyg. **16**:625 (Nov.) 1932.

of the cells, producing dislocations of the nucleus." It must be assumed that, like the tears and fissures in the brain tissues, the changes in the ganglion cells described—tumefaction, vacuolation and liquefaction—are not artefacts or accidental phenomena but mechanical effects of a strong current.

The phenomena of satellitosis and neuronophagia are also of great interest. They were present not only in the deeper layers of the cortex, where they are somewhat manifest even under apparently normal conditions, but even in the upper cortical strata. The assumption is permissible that a short space of time, about two minutes, between the application of the deadly current and the death of the victim suffices to produce reactive phenomena. It is suggestive that the reactive phenomena not only set in early, but evidently are at play some time after the subject apparently succumbs to the first shock. That is to say, gross reactive cerebral phenomena continue even when the subject appears to be dead. This seems to be in accord with the view of some observers who emphasize that death after an electric shock is only apparent. According to Levy,[19] for instance, spontaneous recovery is not uncommon in man within two minutes following an electric shock. Levy said that a person struck down by an electric shock sometimes spontaneously returns to life within the stipulated period, although the heart has stopped and he is apparently dead; that is, during these two minutes the patient may appear dead, but he can be revived. During this period, a few simpler activities of the brain evidently continue in the form of neuronophagia and satellitosis, and the perivascular spaces of the cerebral blood vessels apparently continue discharging their contents into the subarachnoid space.

While death may be only apparent in cases of a single electric shock, as in accidental or experimental electrocution, this is not true in cases of legal electrocution. According to Spitzka, death in legal electrocution is instantaneous; the vital mechanisms of life—circulation and respiration—cease with the first contact. If one considers that in legal electrocution four shocks are produced, it is not permissible to assume that life is present during the two minutes consumed by the shocks. Yet reactive phenomena are manifest in this short period. They follow the primary changes in the ganglion cells, nerve fibers, blood vessels and pia-arachnoid.

According to the majority of investigators, the electric current travels along the blood vessels. This must inevitably cause their contraction and separation from the surrounding glia, with the formation

19. Levy, quoted by MacWilliam, J. A., in discussion of Legge et al.: Pathological Changes Produced in Subjects Rendered Unconscious by Electric Shock, Proc. Roy. Soc. Med. (Electrotherap. Sect.) **15**:45, 1922.

of the shrinkage space of His already mentioned (fig. 5). The current, however, acts not only on the blood vessels but on the pia-arachnoid and its watery contents, causing distention of the subarachnoid meshes and through them distention of the entire subarachnoid space. It evidently also acts directly on the ganglion cells and on the mass of the cerebral tissue, producing fissuration and other pathologic states already described.

The sequence of the foregoing histologic changes and their sequelae can be traced in animals. By passing strong currents (100 volts) into animals, Jellinek [10] caused a slowly developing paresis and paraplegia of the hind legs, paralysis of the bladder and the rectum and loss of sensibility and of the reflexes. Thirty days later, he demonstrated focal and diffuse degeneration. Some portions of the central nervous system, particularly the posterior columns, exhibited fresh degeneration, while others (the lateral columns) showed a predominance of old degenerative changes. In general, the changes produced by electrocution can be classified as concussion of the brain and the cord, a view expressed by Jaeger [20] on clinical, and by Langworthy [21] on experimental, grounds. Whether produced accidentally, experimentally or legally, the changes in the central nervous system due to electrocution are usually alike and may be as manifest in the brain as they are in the skin, bones or heart. They may heal with the formation of scars and affect any part of the central nervous system, giving rise to a great variety of clinical pictures. Thus Panse,[22] Karnosh,[12] Critchley,[23] Löwenstein and Mendel [24] and others described, as sequelae of accidental electrocution, spinal atrophies, amyotrophic lateral sclerosis, hemiplegias, paraplegias, multiple sclerosis, striatal lesions, psychic disturbances and many other clinical conditions. Löwenstein and Mendel termed the sequelae "encephalomyelosis." However, the changes produced by electrocution are neither pathologically nor clinically characteristic, for they may occur in any lesion of the brain that is associated with an increased intracranial pressure, such as tumors of the brain, fractures of the skull and hemorrhages. The possible exception is the tears in

20. Jaeger, Hans: Ueber Starkstromverletzungen, Schweiz. med. Wchnschr. **2**:1250, 1921.

21. Langworthy, O.: Necrosis of the Spinal Cord Produced by Electrical Injuries, Bull. Johns Hopkins Hosp. **51**:210, 1932.

22. Panse, F.: Die Schädigungen des Nervensystems durch technische Elektrizität, Monatschr. f. Psychiat. u. Neurol. **78**:193, 1931; Ueber Schädigungen des Nervensystems durch Blitzschlag, Monatschr. f. Psychiat. u. Neurol. **59**:323, 1925.

23. Critchley, Macdonald: Industrial Electrical Accidents in Their Neurological Aspect, J. State Med. **40**:459 (Aug.) 1932.

24. Löwenstein, K., and Mendel, K.: Hirnschädigungen durch elektrische Einwirkung, Deutsche Ztschr. f. Nervenh. **125**:211, 1932.

the walls of the large blood vessel, which, as pictured in this contribution, have not been described in any type of cerebral injury.

CONCLUSIONS

In legal electrocution, organic changes take place in the central nervous system.

The changes are generally of the same nature as those seen in concussion of the central nervous system.

The changes, with the possible exception of those in the blood vessels, are not specific, for some occur also in cerebral injuries following fracture of the skull and increased intracranial pressure.

Some changes, such as swelling of the ganglion cells and satellitosis, are reparable. Other changes, such as tearing of the brain tissues and of the blood vessels, are irreparable.

Regardless of the apparent death of an electrocuted person, some simpler, primitive functions of the brain (glial reaction and draining of the perivascular spaces by the subarachnoid space) continue for a very short time.

HEMORRHAGE INTO GLIOMAS

A REVIEW OF EIGHT HUNDRED AND THIRTY-TWO CONSECUTIVE VERIFIED CASES OF GLIOMA

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CHICAGO

In Osler's textbook of medicine [1] appears the following statement: "Gliomas (of the brain): They are usually very vascular and the vessels are very liable to degeneration with resulting hemorrhage, thrombosis and edema. This often accounts for acute features appearing suddenly." Most students who have been graduated from medical colleges in recent years have read this statement and accepted it. It has become a widespread belief that gross hemorrhage into gliomas is common. Whenever there is a sudden onset or an acute exacerbation of symptoms in a case of tumor of the brain the possibility of hemorrhage comes first to the minds of many, and occasionally contraindications to operation are based on the theory that decompression is likely to permit such hemorrhage to assume fatal proportions.

To one whose ideas on this matter were no exception to the general rule, it was of considerable interest to encounter in the clinic of Dr. Harvey Cushing, the report of the following, with its significant "special note."

CASE 1.—*Acute development of right hemiparesis and aphasia. Choked disks. Operation with subtotal removal by suction of degenerated glioma. Subsequent discharge from hospital.*

History.—Mrs. L. P., a housewife, aged 48, who was admitted on Jan. 20, 1927, on the recommendation of Dr. Isadore Abrahamson of New York, had been well until six weeks before admission, when she began to have an occasional "sleepy feeling" in the right hand. Two weeks later she noticed suddenly, after taking a bath, that the right side of the face drooped, and the right arm and leg became weak; this was accompanied by twitching of the right arm. No aphasia was apparent at that time, and the patient, after a short stay in bed, recovered completely except for slight residual weakness in the arm. However, one evening, a week before admission, the mouth began drawing toward the left, and the next morning, after she had been awakened with a severe headache, there developed, within the space of one hour, a complete right hemiplegia with aphasia.

Examination.—The patient was apathetic, aphasic and disoriented, and had bilateral choked disk of 2 diopters and slight right abducens palsy. There was

Read at the Fifty-Ninth Annual Meeting of the American Neurological Association, Washington, D. C., May 11, 1933.

1. Osler, William: The Principles and Practice of Medicine: Designed for the Use of Practitioners and Students of Medicine, ed. 11, revised by Thomas McCrae, New York, D. Appleton and Company, 1930, p. 1037.

a right spastic hemiparesis, with questionable hypesthesia on that side. Roentgen examination of the skull showed nothing abnormal.

The patient was operated on by Dr. Cushing on February 4; his special note on the day before operation included the following statement: "Her history was rather an acute one, so that there is little wonder that Dr. ——— may have been inclined to think that she had been stricken with apoplexy. However, the symptoms did not come on suddenly; and the case behaved much more like a thrombosis, which I presume is the actual happening—namely, that some of the large vessels in the center of this spongioblastoma were finally occluded, with a large area of necrosis. There were increased symptoms, and the patient behaved much as would a patient with hemorrhage in a tumor. A large hemorrhage in a tumor, in my experience, is an extremely uncommon thing."

Operation.—A soft, necrotic, markedly degenerated tumor was removed nearly in entirety by suction. There were no hemorrhages in it, but a note was made of many blackish, thrombosed vessels. Histologically, the tumor was difficult to classify, but it was finally placed among the fibrillary astrocytomas.

Of the weight of the opinion of Dr. Cushing there can be no question. As it contradicts a generally accepted belief, it was thought that the study of a sufficiently large number of gliomas, verified by operation or by autopsy, would decide the matter with some authority. With this in mind, the histories of 832 consecutive verified cases of glioma from Dr. Cushing's series at the Peter Bent Brigham Hospital have been reviewed.

A search of the literature for similar studies has shown a paucity of statistical information. Many pathologic descriptions mention the well known tendency of infiltrating gliomas toward microscopic interstitial extravasations of blood. Petechial hemorrhages have been noted, and occasionally a case of massive hemorrhage has been described, giving rise, perhaps, to the statement quoted from Osler, which was made when the total number of reported gliomas was insignificant according to present day standards. No actual figures, however, have been discovered except those given in 1927 by Wilson,[2] in whose series of 35 cases of glioma 9 showed signs of recent hemorrhage of varying amount.

The series reported, therefore, has been reviewed with the object of gathering statistics on gross hemorrhage into gliomas of the brain, with or without attendant clinical symptoms. Those cases in which the extravasation of blood has been microscopic or has limited itself to a few petechiae have been rejected. The 832 cases, classified according to the scheme of Bailey and Cushing,[3] have been studied by groups

2. Wilson, D. C.: The Value of the Blood Picture in the Diagnosis of Glioma with Hemorrhage, Clifton M. Bull. **13**:117, 1927.

3. Bailey, Percival, and Cushing, Harvey: A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis, Philadelphia, J. B. Lippincott Company, 1926.

and the results for the different types as well as for the series as a whole are given in table 1.

Perusal of this table yields several interesting points of information. First, gross hemorrhage into glioma is not common. A 1:27 chance of its occurrence cannot be considered high, although it is not to be disregarded. Again, variations in the frequency of hemorrhage are brought out among the different types of tumor; thus, massive hemorrhage occurred in 5.6 per cent of the cases of glioblastoma, in 5.4 per cent of the cases of astroblastoma and in 10.3 per cent of the cases of oligodendroglioma, whereas it occurred in only 1 of 164 cases of fibril-

TABLE 1.—*Classification of Cases into Groups According to the Type of Tumor and the Presence of Hemorrhage*

Classification of Tumors	Total Number of Cases	Number in Which Gross Hemorrhage Occurred	Percentage in Which Hemorrhage Occurred
Astroblastomas*	37	2	5.4
Astrocytomas, fibrillary	164	1	0.6
Astrocytomas, protoplasmic	91	2	2.2
Atypical	27	4	14.8
Badly preserved	5	1	20.0
Cystic fluid*	52	1	1.9
Degenerated	12	0	0
Ependymoblastomas	9	0	0
Ependymomas	14	0	0
Ganglioneuromas	3	0	0
Glioblastomas	216	12	5.6
Insufficient tissue	42	1	2.4
Medulloblastomas	83	1	1.2
Medullo-epitheliomas	2	1	50.0
Neuro-epitheliomas	2	0	0
Oligodendrogliomas	29	3	10.3
Pineoblastomas	2	0	0
Pinealomas	8	2	25.0
Spongioblastomas	29	0	0
Transitional	5	0	0
Totals	832	31	3.72

* In this group, verification was made by obtaining cystic fluid only; no solid tissue was obtained.

lary astrocytoma. Evidently the more rapidly growing, degenerative lesions are more susceptible to hemorrhage. Cysts, which one might consider particularly vulnerable to hemorrhage, were surprisingly immune, only 1 instance being found of the mixing of fresh blood with cystic fluid.

Gross hemorrhage having been found to occur in 31 of 832 cases, the next question that arose was whether or not there were accompanying symptoms. In a certain number of instances such symptoms were present, as is illustrated by the two cases that follow.

CASE 2.—*Four weeks' history of rapidly developing headache, vomiting, drowsiness, choked disk and left lower facial weakness. Rapid failure and death in the hospital without operation. Autopsy observation of recent large hemorrhage into astroblastoma.*

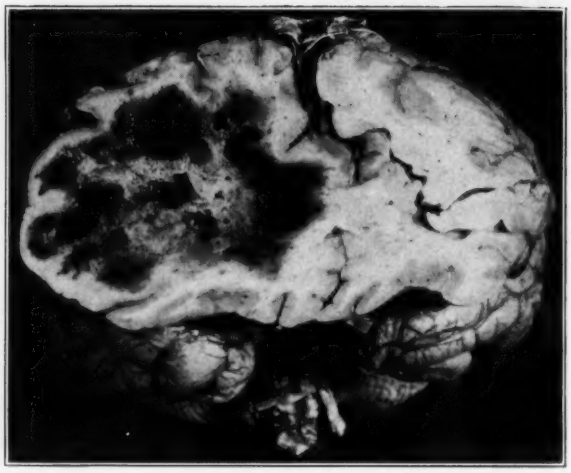

Fig. 1 (case 2).—Right frontal astroblastoma, with hemorrhage.

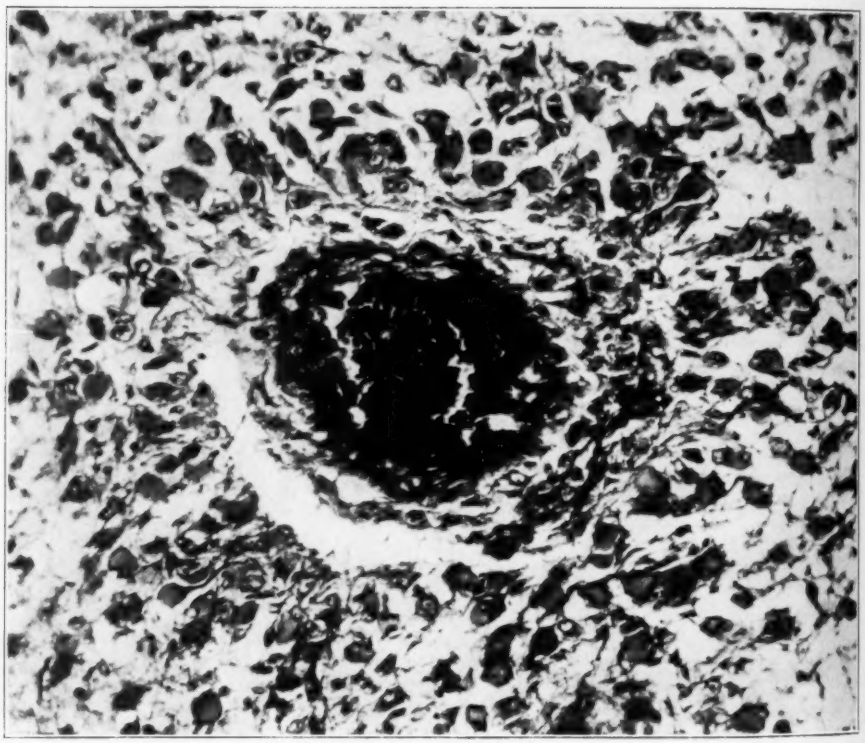

Fig. 2 (case 2).—Section of the tumor shown in figure 1. Note the perivascular arrangement of the tumor cells. Phosphotungstic acid-hematoxylin; × 300.

History.—Mrs. K. M. P., aged 54, who was admitted on April 10, 1927, on the recommendation of Dr. F. L. Taylor of Roxbury, Mass., had been perfectly well until four weeks before admission, when she began to complain of constant ache in the back of the neck. This was later associated with vomiting and drowsiness and caused her to become bedridden. One week before admission her speech became slow, and it was noticed that she used the left hand less than the right. The husband related a vague story about convulsive attacks which were apparently not focal but resembled petit mal.

Examination.—The blood pressure was 160 systolic and 100 diastolic. There were choked disks of 5 diopters and left lower facial weakness. Roentgen examination showed signs of moderately increased intracranial pressure and downward and backward displacement of the pineal body.

Course in Hospital.—During the patient's stay in the hospital the blood pressure rose to 200 and then suddenly fell to 150, during which she became unconscious, and Cheyne-Stokes respiration developed. Also at this time she exhibited curious movements, occurring every fifteen seconds, during which she seemed to be attempting to rotate the head and the upper part of the body to the left. She died two days after admission, respiration ceasing one minute before the heart stopped.

Autopsy.—There were numerous hemorrhages of recent origin, varying from 1 to 4 cm. in diameter, in a large right frontal astroblastoma.

In the next case also, death was apparently hastened by a vascular accident.

CASE 3.—*Operation elsewhere one year before admission, with partial extirpation of midline cerebellar medulloblastoma. Subsequent roentgen therapy. Death shortly after admission, without operation. Autopsy revealed a large hemorrhage in the tumor and around the brain stem.*

History.—K. J. B., a girl, aged 9 years, was admitted on July 2, 1925, on the recommendation of Dr. Kenneth McKenzie of Toronto, Canada, who had operated on her one year before, exposing and verifying a midline cerebellar medulloblastoma. The patient's symptoms disappeared after this procedure, and she was given intensive roentgen therapy. A few weeks before admission, however, there were signs of a recurrence.

Examination.—The girl was acutely ill, with backward retraction of the neck and a respiratory rate of 12. There was marked suboccipital and cervical tenderness, and pressure in this region caused pain in the eyes and increase in the headache. The fundi showed 3 diopters of choking superimposed on a secondary atrophy. There were slight right abducens palsy, nystagmus, ataxia, dysarthria, dysphagia and generalized hypotonicity. The deep reflexes were hyperactive, and there was a bilateral sustained ankle clonus. The child was incontinent.

Course.—Following admission, the patient had several sinking spells, during one of which it was necessary to resuscitate her by artificial respiration. She died of respiratory failure in two days.

Autopsy.—There was a large circumscribed midline cerebellar tumor in which a large blood clot was found. There was also a large amount of clotted blood surrounding the brain stem and even extending up over the cerebral hemispheres.

One might conclude from a study of the foregoing protocols that spectacular symptoms are to be expected when a hemorrhage takes

place in a glioma. With this in mind, the 31 cases in which hemorrhage was proved either at operation or at autopsy were reviewed. In only 7 of the 31, or 0.84 per cent of the entire group of 832, were there any striking features such as sudden onset or acute exacerbation of symptoms. The other 24 progressed as do ordinary cases of glioma in which there is no indication of hemorrhage. On the other hand, in going over the histories of the nonhemorrhagic cases, many examples were encountered in which the clinical changes were as critical as though hemorrhage had taken place. Two will be described in detail.

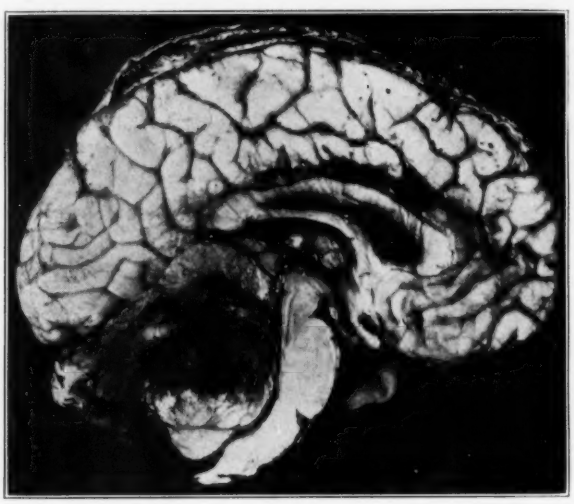

Fig. 3 (case 3).—Hemorrhage into a medulloblastoma. One year before death an operation was performed, followed by intensive roentgen treatment.

CASE 4.—*Sudden development of difficulty in cerebration with subsequent left hemiparesis. Operation with removal of cystic right frontal glioblastoma. Death. Autopsy.*

History.—Mrs. S. S. H., aged 52, who was transferred from the medical to the surgical service on Nov. 27, 1929, having been recommended by Dr. Angus D. Black, of Brattleboro, Vt., had been well until ten weeks before admission to the medical service. At that time, after lying on a couch resting, she rose and walked a few feet; she suddenly felt weak and was forced to sit down. On attempting to talk she could do no more than make some gurgling noises in the throat. Later that day, she began to have twitchings in the hands, and it was noticed that the left side of the mouth drew downward and outward, and that saliva ran from it. The blood pressure, taken on that day by the family physician, was 150 systolic and 80 diastolic. During the next few days, the left facial paresis and the difficulty in talking apparently disappeared. At no time was there headache or vomiting, and the patient seemed well until six weeks later, when she suddenly experienced difficulty in speaking and cerebration, and became dull and apathetic.

Examination.—When admitted to the medical service, the fundi were normal except for slight blurring at the edge of the disk on the left. There were a bilateral positive Babinski sign, bilateral unsustained ankle clonus, left facial paresis and semistupor. The blood pressure on admission was 168 systolic and 88 diastolic, but this dropped, and frequent readings varied between 140 and 160 mm. of systolic pressure. While in the medical service, the patient went into deep coma on two or three occasions, with slow respiration and incontinence. Choked disks eventually developed, and the patient was transferred to the surgical service.

Neurologic Examination.—At this time the patient was still semistuporous, and did not speak voluntarily or answer questions. There were a left hemiparesis and bilateral choked disk of 0.5 diopters. The deep reflexes were increased on the left. The Wassermann test of the blood was negative; the blood urea nitrogen was

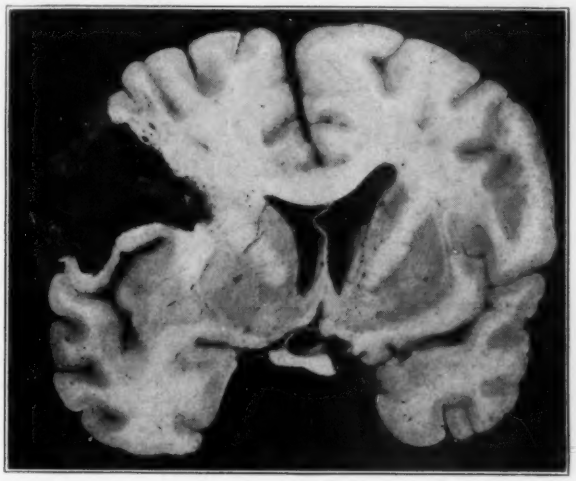

Fig. 4 (case 4).—Coronal section showing the area from which a tumor has been removed. The defect is partially filled with fresh postoperative blood.

low; the urine contained no albumin, and there was only slight sclerosis of the peripheral vessels. Roentgen examination of the skull showed no abnormality.

Operation.—Ventriculography, performed by Dr. Horrax on December 5, indicated a right frontal tumor, and Dr. Cushing on the same day removed, *en bloc*, a surface glioma (glioblastoma, partially cystic), about 4 cm. in diameter, at the lower end of the rolandic fissure.

Autopsy.—The patient died on the following day, and section of the tumor and of the brain revealed no hemorrhage.

CASE 5.—*Sudden onset of right hemiparesis, aphasia and headache. Operation with verification of deep, left-sided glioblastoma. Subsequent roentgen treatment.*

History.—D. L., a broker, aged 52, who was admitted on Dec. 6, 1928, on the recommendation of Dr. Israel Wechsler, of New York, had been well until six months before admission, when suddenly, while at lunch, right hemiparesis developed which was so complete that he could not get up from the table and could not use the right hand. At the same time a warm feeling passed over the right side, the arm and leg became numb, and he became paraphasic. After remaining in bed for three or four weeks, he improved sufficiently to walk, but with a marked

drag of the right foot. For a month before admission, however, there had been a return of the original symptoms.

Examination.—The fundi were normal. The blood pressure was 120 systolic and 80 diastolic. The characteristic symptoms of a right sensorimotor hemiparesis were observed. Roentgen examination of the skull showed nothing abnormal.

Course.—During the patient's stay in the hospital, he began to complain of smelling imaginary bad odors, and choked disks of 1 diopter developed.

Operation.—On December 17, Dr. Cushing found a tumor at a depth of 5 cm. beneath the left supramarginal gyrus. Tissue taken for verification showed a glioblastoma multiforme. The patient was given subsequent roentgen treatment and was discharged from the hospital. Four months later, he died, and autopsy was not obtained. At the time of the operation, however, there was no evidence of hemorrhage in or around the tumor.

COMMENT

It would appear, then, that one can say that hemorrhage into a glioma is uncommon, that it occurs in association with extraordinary symptoms in less than 1 per cent of all cases of glioma, and that the acute manifestations for which it is infrequently responsible may also appear in patients with tumors in which there has been no hemorrhage. The latter possibility has been noted by many writers and has been well discussed in recent years by Globus and Strauss.[4] There is a multiplicity of causes for it. One of them is that these lesions have a tendency, as noted by Riley and Elsberg,[5] to occlude cerebral vessels rapidly, with resultant degeneration. Again, tumors strategically situated may shut off a foramen of Munro or the aqueduct of Sylvius and so occasion sudden phenomena. Acute edema may occur, rather unaccountably, around and in a glioma, particularly when it is cystic. Less commonly, the dramatic beginning of the clinical history may be an unrecognized focal seizure, mistaken for an apoplectiform attack, with residual neurologic findings. At any rate, it is clear that many factors make a certain diagnosis of hemorrhage developing into a tumor of the brain difficult and often impossible.

This is one reason why objection to operation because of the possibility of increasing hemorrhage is based on insecure ground. Even if decompression were extremely prone to promote this catastrophe, its comparative rarity and the complications in the way of hypothecating it would minimize the risk involved.

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4. Globus, J. H., and Strauss, I.: Vascular Lesions and Tumors of the Brain: Difficulties in Differential Diagnosis, Arch. Neurol. & Psychiat. **15**:568 (May) 1926.

5. Riley, H. A., and Elsberg, C. A.: Differential Diagnosis Between Cerebral Degeneration, Infiltrating Cerebral Neoplasm and Infiltrating Cerebral Neoplasm with Degeneration, Arch. Neurol. & Psychiat. **15**:48 (Jan.) 1926.

Does decompression facilitate the development of hemorrhage into a glioma? In 22 of the 31 cases of hemorrhage, decompression had been done prior to the operation or the necropsy at which the lesion was found. Case 3 is a case in point, though in it there is the complicating feature of intensive roentgen treatment. The following cases perhaps illustrate better that decompression may be a contributing factor.

CASE 6.—*Two months of headache, vomiting, right-sided weakness, tinnitus in the right ear and hallucinations of smell and vision. Choked disk. Decompression. Death within a few hours.*

History.—Mrs. E. W., aged 39, who was admitted on Sept. 20, 1916, on the recommendation of Dr. F. S. Guild of Mattapan, Mass., two months before admission had begun to have headache, vomiting and pain in the back of the neck. She

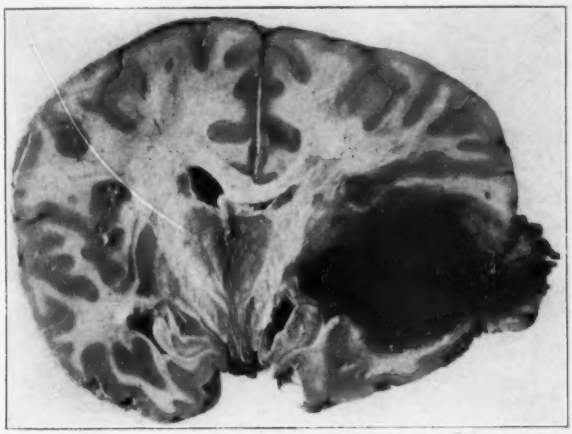

Fig. 5 (case 6).—Right temporal glioblastoma, with hemorrhage.

complained one evening of smelling a "gassy" odor, which was not present in the room, and on subsequent occasions smelled imaginary disagreeable odors. During this same period, she frequently had the illusion of seeing a hand arrange something in a show-case in front of her. Six weeks before admission, she noticed weakness in the right leg, and three weeks later numbness in the right side of the face. On admission, she was sleepy and stuporous, and her husband said that her speech had been slow for three or four days.

Examination.—The blood pressure was 125 systolic and 80 diastolic. There were bilateral choked disk of 5 diopters, slight left facial weakness and right hemiparesis.

Operation.—Two days after admission, a right subtemporal decompression was done by Dr. Horrax.

Autopsy.—The patient died in the evening following the operation. Section of the brain revealed a large infiltrating glioblastoma of the right temporal lobe in which were three fairly large hemorrhages.

CASE 7.—*Convulsive attacks for seven years, with gradually developing change in personality; choked disk; aphasia. Operation with tapping of cyst and decompression. Death. Autopsy.*

History.—Miss M. M., aged 18, who was admitted on April 6, 1920, on the recommendation of Dr. Smith E. Jelliffe of New York, seven years before admission, had had a fainting spell during which she was unconsicous for an hour. Following this she seemed well until four years before admission, when she had several generalized convulsions lasting from three to four minutes, associated with vomiting and followed by drowsiness and headache. After a seizure, she was frequently unable to speak for several minutes and often could not remember well known facts or the whereabouts of familiar objects. Three years before admis-

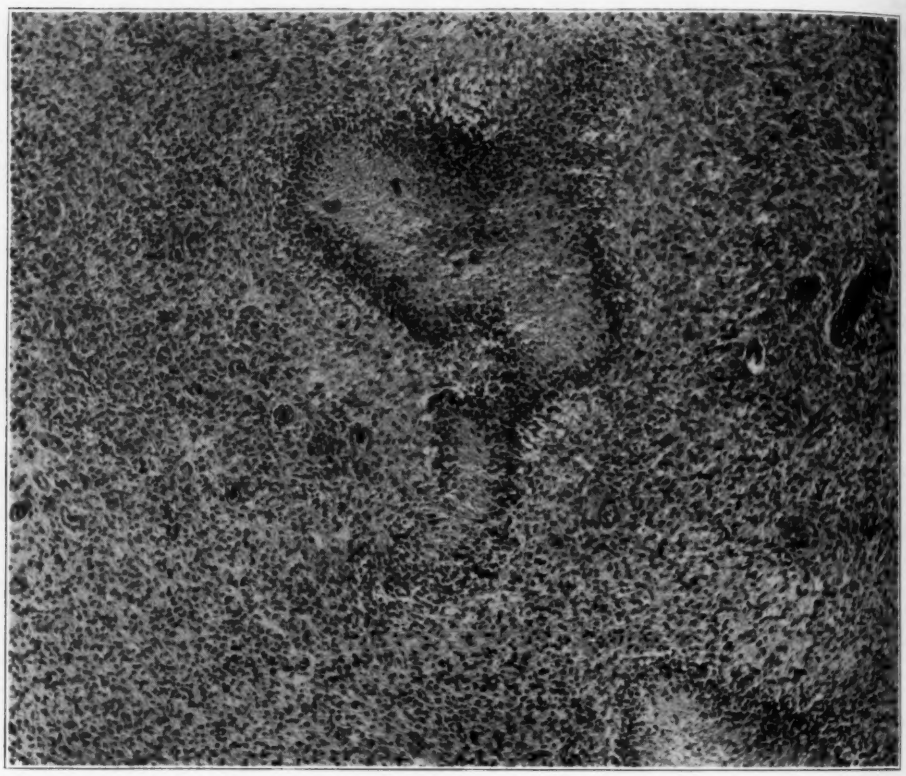

Fig. 6 (case 6).—Section of the tumor shown in figure 5. Note the pseudopalisading characteristic of degeneration. Hematoxylin and eosin; × 80.

sion, she began to show considerable mental aberration, manifesting itself in the form of extreme lack of inhibition in sexual propensities. A year and a half before admission, the patient was comparatively normal for from six to eight months, but she then became arbitrary, arrogant and dictatorial, and was given to violent tantrums during which she lay on the floor and rolled in her own vomitus. At the same time she began to have severe headache, rigidity of the neck and unsteadiness of the arms and legs. Four months before admission, bilateral hyperemic fundi were noted by Dr. Wilmer in Baltimore, and at this time the patient also had diplopia. Failing vision, bilateral exophthalmos and ptosis of the left eyelid soon developed, after which the patient was admitted to the hospital.

Examination.—The blood pressure was 90 systolic and 65 diastolic. There were loss of sense of smell and complete blindness, with 4 diopters of choking superimposed on secondary optic atrophy. There were anomia, right lower facial weakness and right hemihypesthesia.

Operation.—Dr. Cushing performed a left subtemporal decompression and tapped a cyst containing 20 cc. of xanthochromic fluid, which clotted.

Autopsy.—The patient died four weeks later. A large left-sided glioblastoma was disclosed, into which there had been massive hemorrhage.

That in 22 of the 31 cases decompression had been performed may appear at first glance like circumstantial evidence against operation. It must not be forgotten, however, that decompression was

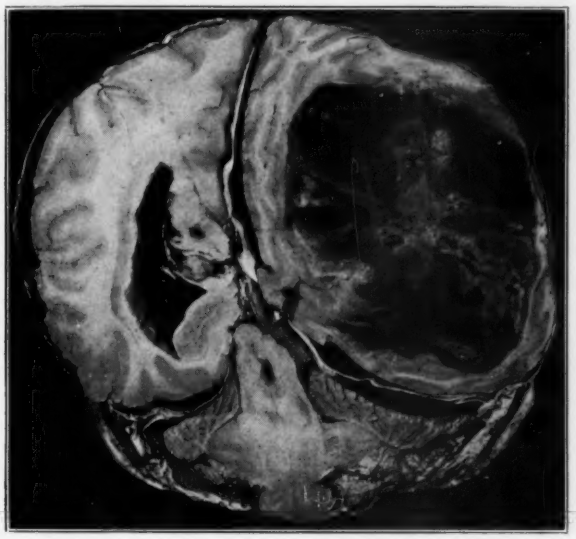

Fig. 7 (case 7).—Coronal section, showing hemorrhage into a glioblastoma of the left hemisphere.

done in all of the remainder of the entire series of 832 without fatal accident as far as hemorrhage was concerned, except in the few cases which came to autopsy without operation. This fact, plus the evidence which has been presented showing the small percentage of cases in which hemorrhage betrays itself clinically, and the diagnostic hazards which are present in certifying such an accident, should serve to make a contraindication to operation on such a basis a negligible factor.

A few interesting incidental findings should be reported, for which the data are given in table 2. In the 31 cases of hemorrhage, there were 15 males and 16 females, the average age being 34½. The blood pressure was recorded in 17 instances, and was well within normal range in all but 2, as was true of the 9 cases reported by Wilson.[2] Seven

patients in the series were children, in all of whom the hemorrhage was in midline or near midline tumors. For the group of 31 as a whole, however, the percentage of tumors in this location was 38.9 per cent, which corresponded exactly with the proportion for the entire series of 832. The Wassermann test of the blood was negative for all patients for whom it was determined. In other words, no evidence could be adduced which would serve to distinguish the type of case liable to hemorrhage from the ordinary case of glioma.

TABLE 2.—*Incidental Findings in Thirty-One Cases of Hemorrhage*

Patient	Age	Sex	Type of Tumor	Location of Tumor	Blood Pressure		Presence of Decompression Before Verification of Hemorrhage	Presence of Suggestive History
					Systolic	Diastolic		
W. M. B.	41	M	Astroblastoma	Left frontal	128	74	+	+
K. M. P.	54	F	Astroblastoma	Right frontal	160	100	—	+
E. W. L.	38	F	Astrocytoma, fibrillary	Left frontal	110	90	+	—
E. T. B.	43	M	Astrocytoma, protoplasmic	Corpus callosum	...	...	+	—
E. M.	53	F	Astrocytoma, protoplasmic	Left temporal	136	85	+	+
G. W. B.	58	M	Atypical	Left temporal	125	58	—	—
A. F. F.	41	M	Atypical	Right recess	125	95	—	—
S. A. G.	17	M	Atypical	Left occipital	110	78	—	—
E. R.	20 mo.	F	Atypical	Cerebellum	...	...	—	—
R. D. F.	48	M	Badly preserved	Third ventricle	...	...	+	—
A. M. T.	9	F	Presence of cystic fluid	Cerebellum	115	65	—	—
J. R. B.	60	M	Glioblastoma	Right temporal	...	...	+	—
H. H. D.	29	M	Glioblastoma	Thalamus	135	100	+	—
H. D.	69	F	Glioblastoma	Right frontal	135	80	—	—
E. J. E.	61	F	Glioblastoma	Left frontal	170	80	+	—
M. E. F.	32	F	Glioblastoma	Right hemisphere	...	...	+	—
R. C. H.	40	M	Glioblastoma	Left temporal	125	60	+	—
G. A. L.	13	F	Glioblastoma	Pons	100	70	+	—
A. McA.	30	M	Glioblastoma	Right temporal	...	...	+	—
M. M.	18	F	Glioblastoma	Left temporal	...	...	+	—
M. E. O'B.	6	F	Glioblastoma	Pons	...	...	+	—
A. M. S.	49	F	Glioblastoma	Left temporal	...	...	+	—
E. F. W.	39	F	Glioblastoma	Right temporal	125	80	+	+
R. F. W.	33	M	Insufficient tissue	Right hemisphere	110	68	—	+
K. J. B.	10	F	Medulloblastoma	Cerebellum	...	...	+	+
C. B. G.	48	F	Medullo-epithelioma	Pineal	...	...	+	—
K. P. B.	24	M	Oligodendroglioma	Thalamus	...	...	+	—
R. S. D.	40	M	Oligodendroglioma	Right hemisphere	140	90	+	—
R. A. I.	45	F	Oligodendroglioma	Right frontal	115	85	+	—
S. K. B.	12	M	Pinealoma	Pineal	...	...	+	+
L. T.	9	M	Pinealoma	Pineal	...	...	—	—

SUMMARY AND CONCLUSIONS

In a review of this kind there is little to be gained by the lengthy discussion that would be necessary if the study concerned a controversial question. It is, on the contrary, a mere statistical survey of a subject about which there has been much conjecture with little concrete background. The facts obtained have been gathered in the hope of furnishing guidance in the diagnosis and treatment of puzzling cases of tumor of the brain in which the symptoms seem to indicate a sudden change in the character of the suspected lesion. While they refute what seems to have been a cherished conviction on the part of many, it is probable

that the misapprehension had its origin in the lack of opportunity for observation of a sufficient number of cases from this angle. This review attempts to fulfil that need. Its results justify the following conclusions:

1. Spontaneous massive hemorrhage occurred in 31, or 3.7 per cent, of 832 cases of glioma, being somewhat more common in rapidly growing varieties and less common in slowly growing ones.

2. The 31 cases in which gross hemorrhage occurred did not differ from the series as a whole in respect to age, sex, blood pressure or location of the glioma.

3. Hemorrhage was accompanied by appropriate clinical symptoms in only 7, or 0.84 per cent, of the 832 cases.

4. The same type of symptoms may appear in cases of glioma in which there has been no hemorrhage.

5. Only a dubious diagnosis of hemorrhage into a glioma in the presence of the sudden onset or acute exacerbation of symptoms of tumor of the brain can therefore be made.

6. Accordingly, contraindications to operation should not be based on such an assumption because of the comparative rarity of the condition, because of the reasonable doubt in its diagnosis and because there is no evidence to show that operation is unduly hazardous in a significant number of cases.

DISCUSSION

DR. WALTER F. SCHALLER (San Francisco): This paper is very valuable as a statistical study of verified material. It has been the fashion of late to diagnose hemorrhages in cases of suspected gliomas which have eventuated in sudden cerebral accidents and have shown obscure symptoms and signs but no pathologic cardiovascular background. So few of the reported cases, relatively speaking, have shown spontaneous hemorrhages that frequent mistakes in diagnosis have undoubtedly been made. I have a case to report of a child who died thirteen and one-half hours after a diagnostic lumbar puncture and removal of 4 cc. of lumbar fluid. No adverse symptoms occurred until thirteen hours after the tap, when the child had a convulsion and showed signs of bulbar failure. Death occurred half an hour later.

The cause of death was a hemorrhage in the anterior part of the thalamus. This case may then be included in the classification of Dr. Oldberg's series of cases of decompression.

MYELITIC AND MYELOPATHIC LESIONS

VI. CASES WITH MARKED CIRCULATORY INTERFERENCE AND A PICTURE OF SYRINGOMYELIA

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AND
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Myelopathy due to extramedullary or intramedullary expanding lesions may lead to cavity formation—syringomyelia. Clinically, such cases are sometimes erroneously regarded as true syringomyelia. The myelopathic process and the secondary cavity formation may be due to: (1) destruction of tissue of the cord by an intramedullary tumor; (2) circulatory interference within the cord from compression of the intraspinal vessels by an intramedullary tumor, or (3) circulatory interference by direct compression of the cord and its vessels by thickened meninges or by an extramedullary neoplasm or by both. In some cases the pathologic process may be due to a combination of all these factors. This type of cavity formation in the cord is not to be confused with true syringomyelia, which is usually attributed to congenital developmental anomalies of the cord with dilatation of its central canal or to a central gliosis which may be due to nests of glia cells or of embryonal nests which may proliferate under the influence of some trauma or irritant in persons with congenital predispositions.

REPORT OF CASES

CASE 1.—*History.*—B. F. L., a woman, aged 61, was admitted to the hospital on July 30, 1920, with the history that in 1910 motor and sensory signs and symptoms of an intramedullary lesion in the cervical cord developed, which was thought to be a tumor. One year later she was operated on (Dr. Elsberg), and a diagnosis of intramedullary gliosarcoma of the spinal cord was made. Following the operation tetraplegia developed which gradually improved somewhat, although the disturbances of sensation and atrophy of the left upper extremity persisted. The patient remained in this condition until 1923, when the tetraplegia and the sensory disturbances became aggravated. Occasionally she also had urinary incontinence.

Neurologic Examination.—On admission the patient presented an acromegalic facies, weakness of the central part of the right side of the face and signs of intramedullary disease of the cord between the third cervical and the second dorsal segments.

From the Neuropathological Laboratory, Montefiore Hospital.

Read at the Fifty-Eighth Annual Meeting of the American Neurological Association, June 7, 1932, at Atlantic City, N. J.

Course.—The patient's condition became progressively worse. In February, 1925, decubitus, pneumonia and dysarthria developed. She died on May 5, 1925.

The clinical and anatomic diagnosis was intramedullary tumor of the spinal cord, septicemia and terminal bronchopneumonia.

Necropsy.—Gross Examination: The brain appeared normal. The third, fourth and fifth cervical segments of the spinal cord were occupied by an irregular, egg-shaped, soft, grayish-white tumor, covered anteriorly by a thin layer of cord tissue; below this level the cord was thinned out and soft for a distance of 2 cm. In the cervical region there was a marked accumulation of cerebrospinal fluid in the subarachnoid space.

Microscopic Examination: The cervical segments of the cord on the left side showed invasion by a tumor (fig. 1 *A*), with practically complete distortion and destruction of this portion of the cord. In some areas the dura was extensively thickened (fig. 1 *B*), causing direct compression of the cord and secondary circulatory interference. The intraspinal vessels showed thickening of the walls. Sections of the cord immediately below the preceding one showed cavitation and invasion by the tumor laterally (fig. 1 *C*). The cavity, which involved only two segments, was lined not by ependymal cells but by a band of connective tissue, and was rich in sprouting capillaries. The anterior horn cells showed marked destructive changes. Sections of the cord above and below the tumor showed evidences of ascending and descending demyelinization. Longitudinal sections stained by the Bielschowsky method showed fragmentation of axis-cylinders adjacent to the tumor with preservation of those remote from it. Sections stained with Mallory's phosphotungstic acid showed a poor glial response. The tumor belonged to the glioma group.

The microscopic diagnosis was myelopathy and syringomyelia.

Comment.—The lesions in the cord were apparently due to: (1) destruction of the cord by the intramedullary tumor; (2) direct compression by the thickened dura, and (3) circulatory interference of the vessels of the spinal cord from compression by the tumor and the thickened meninges.

CASE 2.—*History.*—W. R., a boy, aged 14, was admitted to the hospital in April, 1930. At the age of 9 years the parents had noticed that he began to limp and that the left lower extremity was shorter than the right. This was followed by scoliosis three years later, when a diagnosis of poliomyelitis was made. In January, 1930, while walking up the stairs in school he experienced a sudden pain in the back with weakness of both lower extremities and fell, striking his left elbow. He managed to walk home without assistance, but two days later became incontinent and unable to move the left leg or to extend the fingers of the left hand. He was taken to Mount Sinai Hospital (January, 1930) where a complete block at about the fourth cervical segment was found. Laminectomy (Dr. Ira Cohen) disclosed hematomyelia at the fifth cervical segment. Following operation there appeared signs of a complete transverse lesion of the cord at the eighth cervical segment.

General Examination.—On admission to the Montefiore Hospital examination revealed pigeon breast, rapid heart rate (100) and a distended bladder.

Neurologic Examination.—There were: weakness of the upper extremities, more marked on the left; flexion of the fingers of the left hand, especially on the ulnar side; flaccid paraplegia, and generalized muscular wasting. All tendon

reflexes were absent, except for the biceps humeri. There was no Babinski sign. There were diminution of touch, pain and temperature sense from the toes to the sceond thoracic segment on the right and to the eighth thoracic segment on the left, loss of vibration sense from the toes to the hips, and loss of the sense of position in the toes. There was incontinence of urine and feces.

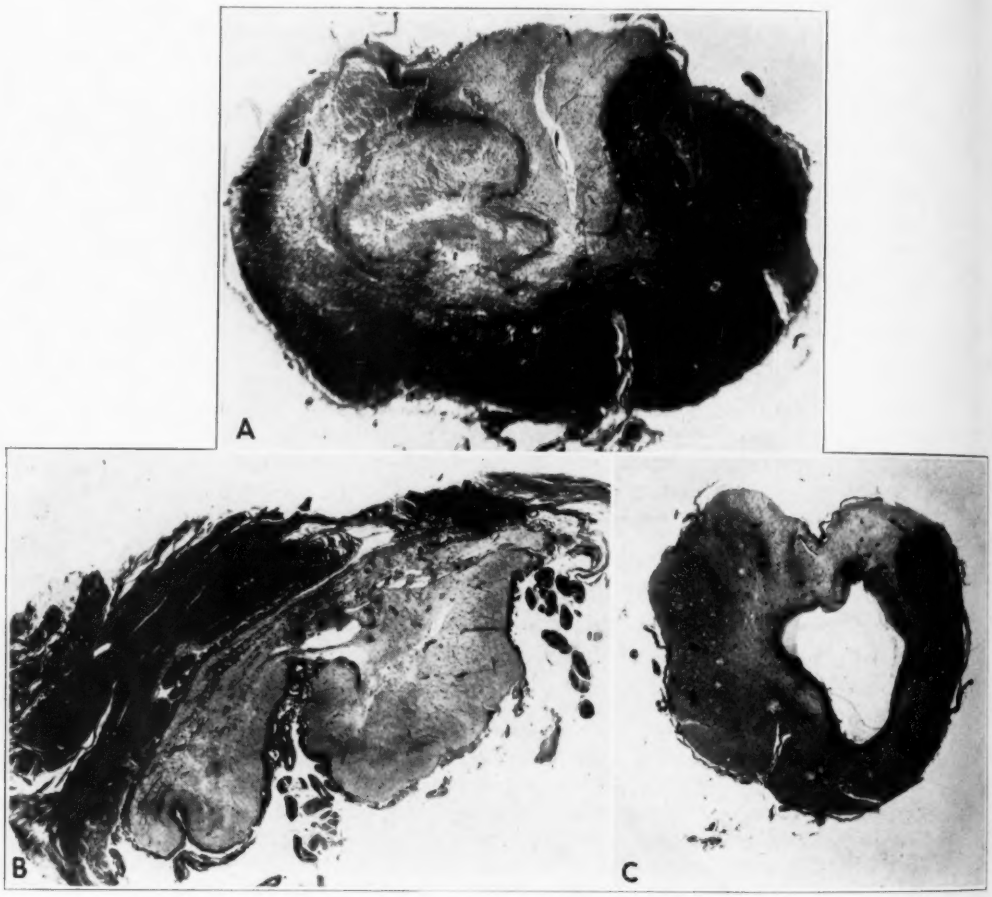

Fig. 1.—*A*, transverse section of the cervical cord showing intramedullary tumor on the left side. *B*, markedly thickened dura destroying half of the substance of the cord. *C*, transverse section showing intramedullary tumor and cavitation. Myelin sheath stain (Weil modification).

Laboratory Data.—At Mount Sinai Hospital (January, 1930) roentgen examination disclosed a scoliosis of the lower dorsal segment. A Queckenstedt test showed a complete block. There was a Froin syndrome. Following the test all the sensory signs disappeared. Injection of iodized poppy seed oil 40 per cent on February 4 by the cisternal route showed a complete arrest of the oil at the

fourth cervical vertebra; following this the sensory impairment returned, with a zone of hyperalgesia between the third and fifth cervical segments.

Course.—At Mount Sinai Hospital, following laminectomy, the patient improved so that he was able to sit in a wheel-chair. In August, 1930, atrophy without fibrillations was noticed over the left thenar, hypothenar and interosseal muscles of the hand. The sensory level at this time was at the seventh dorsal segment. In November, 1930, convulsions developed, and the patient became drowsy and comatose. Examination at this time revealed bilateral papilledema, rigidity of the neck, exaggerated knee jerks, pulse rate of 120, temperature 99.9 F. and blood pressure 200 systolic and 160 diastolic. A lumbar puncture disclosed clear fluid with 160 cells, chiefly lymphocytes, and positive globulin and albumin tests. The urea nitrogen was 59 and creatinine, 1.2. The patient died on November 3.

The clinical and anatomic diagnosis was hematosyringomyelia, intramedullary neoplasm of the spinal cord, scoliosis of the vertebral column, hypertrophied bladder, bilateral hydronephrosis and localized pericarditis.

Necropsy.—Gross Examination: The cord was markedly swollen, especially in the upper dorsal region, and the vessels were engorged. On section, a cavity surrounded by whitish firm tissue was found between the first cervical and the second dorsal segments. The largest diameter of this cavity was between the fifth cervical and the first thoracic segments; it contained blood, and displaced most of the cord (fig. 2). Between the second and third thoracic segments, the bulk of the cord was filled by gelatinous tumor tissue and organized clot. The outer surface of the cord appeared whitish and was of firm consistency. Part of the tumor tissue was found as low down as the first lumbar segment. All lumbar segments contained a slitlike cavity in the anteroposterior diameter of the cord. This cavity assumed larger proportions in the sacral segments, where it replaced the greater part of the cord substance (fig. 2).

Microscopic Examination: In sections stained for myelin sheaths most of the fiber tracts were destroyed (fig. 2). The cavities were lined by endothelial cells. The walls of the cavity in most segments consisted of rows of glia nuclei with few fibers, a layer of proliferated blood vessels and an outer layer of glia fibers. At the tenth dorsal segment the slitlike cavity presented similar histologic features except that the inner wall in one area was lined by ependymal cells. This was the only evidence of a relationship between the tumor cavity and the central canal. Of all structures of the spinal cord, the anterior horn cells, although they showed pathologic changes, were best preserved. In longitudinal sections the myelin sheaths were disintegrated and the axis-cylinders were broken down. The substance of the cord adjacent to the tumor tissue showed an increase in glia. The tumor was a medulloblastoma.

The microscopic diagnosis was myelopathy and hematosyringomyelia.

Comment.—This case also illustrates a syringomyelic cavity due to: (1) destruction of the substance of the cord by an intramedullary tumor, and (2) circulatory interference from the effects of a tumor on the intraspinal vessels of the cord. The meninges were not thickened, so that vascular interference from this source may be excluded. It is noteworthy, though difficult to explain, that in spite of the massive destruction of the tissue of the spinal cord, many of the anterior horn cells were well preserved. The slitlike cavity found between the eleventh

dorsal and the fourth sacral segments was at first thought to be a dilated central canal, but histologic studies showed it to have been produced by the intramedullary tumor.

CASE 3.—*History.*—R. T., a woman, aged 50, was admitted to the hospital on Oct. 13, 1918, with the history that in June, 1918, she noticed weakness of both hands and a feeling of "coolness" in the left hand and in the lower extremities, especially the right. In October, 1918, she complained of vague pains over the entire body, diminished sensation in the extremities, general weakness, difficulty in walking and dyspnea.

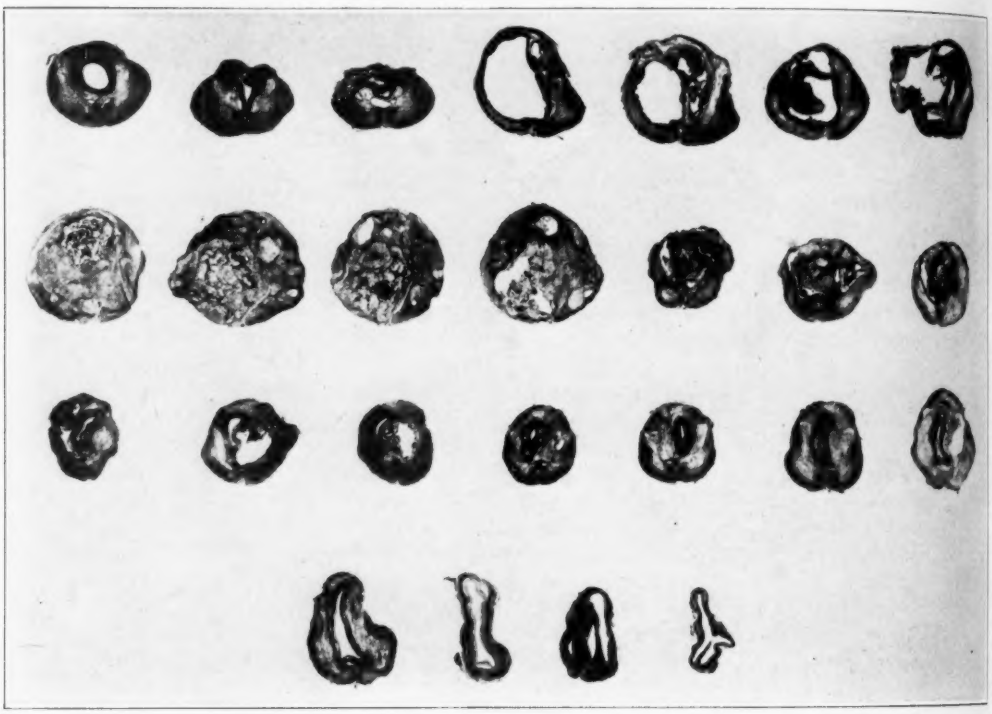

Fig. 2.—Transverse sections of the cord from the first cervical to the fourth sacral segments showing: syringomyelic cavity from the fifth cervical to the first dorsal segments, inclusive; intramedullary neoplasm of the cord between the second and the tenth dorsal segments, and a slitlike cavity from about the first lumbar to the fourth sacral segments which became enlarged in the sacral region. Myelin sheath stain (Weil modification). The sections are as follows: Row 1 (top, left to right), first, second, third, fifth and sixth cervical segments and first and second dorsal segments. Row 2 (left to right), third, fourth, fifth, sixth, eighth, ninth and tenth dorsal segments. Row 3 (left to right), eleventh and twelfth dorsal segments and first, second, third, fourth and fifth lumbar segments. Row 4 (left to right), first, second, third and fourth sacral segments.

Neurologic Examination.—The right pupil was larger than the left; both were irregular, but reacted promptly to light and in accommodation. There were atrophy of the right deltoid and of the intrinsic muscles of both hands, more marked on the right; weakness of both hands, and *"main en griffe,"* with pseudo-athetoid movements of the fingers of the left hand. The reflexes of the upper extremities were hyperactive, except for the right biceps which was diminished; the knee jerks were exaggerated; the ankle jerks were diminished, and there was a bilateral Babinski sign; the abdominal reflexes were not elicited. There were marked scoliosis, with tenderness on percussion over the spinous processes of all vertebrae, and marked cyanosis of the distal ends of the extremities. There was a suggestion of a zone of hyperalgesia between the second and fifth dorsal segments, below which there was hypalgesia, more marked on the left, reaching as far as the fifth lumbar segment, and analgesia and loss in vibratory sensation below this to about the sulcus of the buttocks. Tactile sensibility was unimpaired, and there was dissociation of thermal sensibility between the fifth dorsal and the fifth lumbar segments on the left. Deep muscle sense was diminished in the left upper extremity.

Laboratory Data.—Roentgen examination showed transparency of the bodies of the fourth, fifth and sixth and of the left half of the bodies of the ninth and tenth thoracic vertebrae. All other laboratory findings were negative.

Diagnosis.—Clinically, the diagnosis rested between progressive degenerative intramedullary disease of the cord of the nature of syringomyelia, gliosis or arteriosclerosis of the cord. The anatomic diagnosis was syringomyelia, pulmonary emphysema, purulent bronchitis, decubitus ulcer and terminal pulmonary edema.

Necropsy.—Gross Examination: Except for shrunken gyri, the brain showed no abnormalities. There was lordosis of the vertebral column involving the second, third, fourth, fifth and sixth dorsal vertebrae. In the cervical region the dura and pia-arachnoid were markedly thickened and adherent to the cord. The dura over the lower third of the cord was bulging, and when the dura and the pia were incised about 30 cc. of thin, dark, blood-tinged fluid escaped. There were considerable differences in the circumference of the cord at various levels. There was canalization throughout the cord, extending to the upper half of the medulla oblongata. In the lower lumbar region, which appeared moderately hollowed out, the white and gray matter showed distortion. The central canal was surrounded by a thin, gray translucent zone. In the midportion of the medulla oblongata there was also some "hollowing out" around the central canal; the fiber tracts of the medulla oblongata appeared translucent.

Microscopic Examination: With the myelin sheath stain the outline of most of the segments of the cord was markedly distorted (figs. 3 *A* and *B*), although occasionally some of the white and gray matter could be distinguished. Under a higher magnification, the myelin sheaths of some of the tracts appeared fairly well preserved, the remaining ones being destroyed and replaced by glia. Most sections of the cord showed with the hematoxylin-eosin stain a cavity without ependymal lining, except in one section from the cervical region (fig. 4) in which the cavity was in direct communication with the central canal, an end-result of destruction of the substance of the cord near the canal. The wall of the cavity was surrounded by a slight glial proliferation. The meninges were markedly thickened, especially in the ventrolateral portions of the cervical region (fig. 3 *A*). The vessels of the cord proper showed extensive thickening, especially of the adventitia, but no round cell infiltrations. The anterior spinal arteries were thickened and

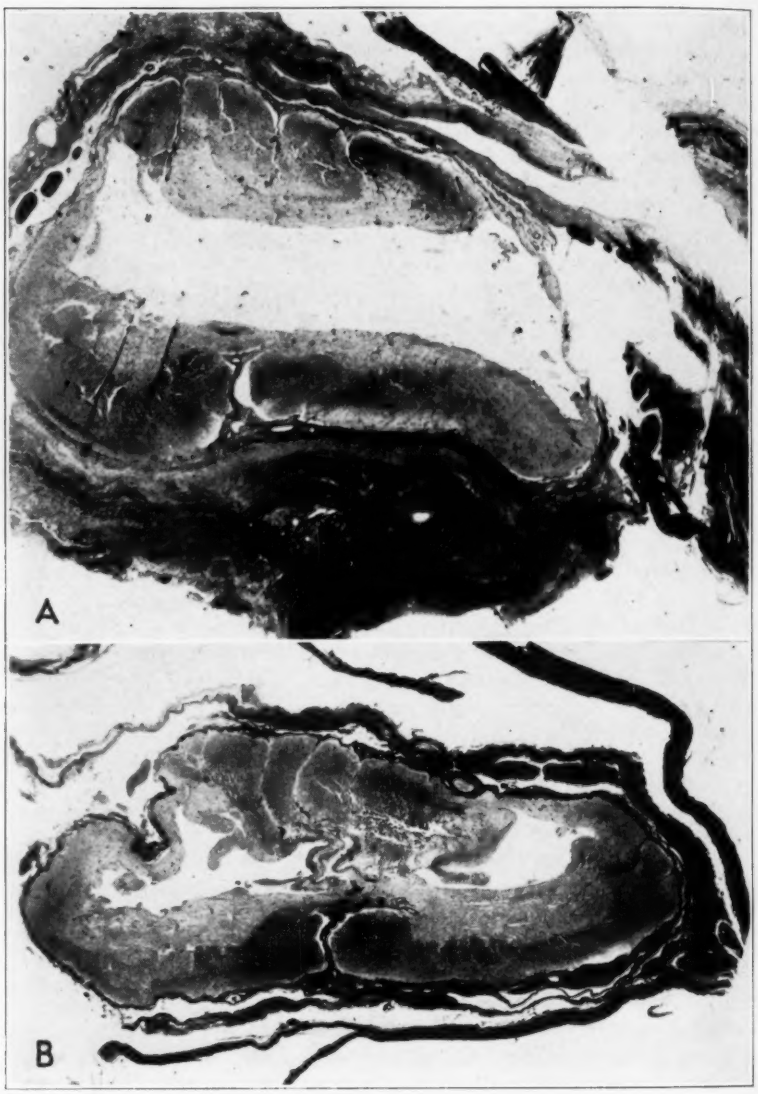

Fig. 3.—*A*, thickened and adherent dura in the cervical region; cavitation and destruction of the cord. *B*, transverse section of the thoracic region showing destruction of the cord and cavitation. Myelin sheath stain (Weil modification).

had narrow lumens. Numerous psammoma bodies were present between the dura and the pia-arachnoid. With the Nissl stain, the anterior horn cells appeared completely destroyed in some areas, but in others, especially where the cord was intact, they were well preserved. Longitudinal sections stained for myelin sheaths showed complete demyelinization of the fiber tracts. The myelin sheaths took the stain poorly, some of them appearing completely destroyed and swollen. Bielschowsky's preparations showed almost complete destruction of the axis-cylinders. In sections stained with Mallory's phosphotungstic acid slight glial response was observed in some areas. In the area of destruction there was hardly any attempt at repair noticeable.

The microscopic diagnosis was myelopathy and syringomyelia.

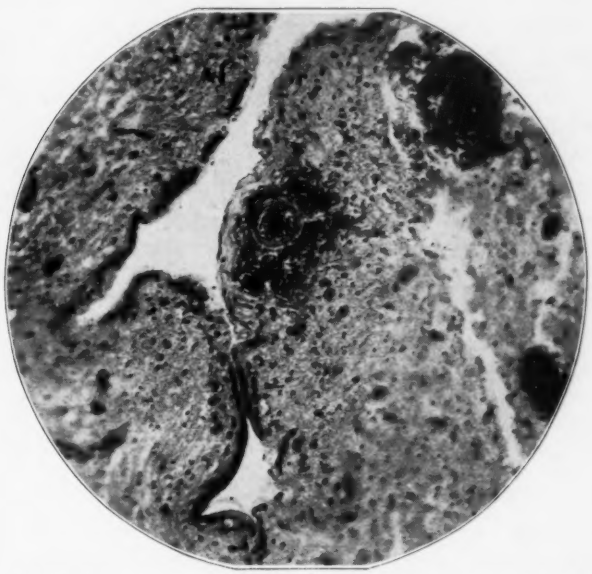

Fig. 4.—Partially lined cavity with ependymal cells. The syrinx was in direct communication with the central canal, the end-result of breaking down of cord substance near the central canal. Hematoxylin-eosin stain; × 100.

Comment.—The marked thickening of the meninges was most likely the cause of the changes in the cord (distortion, destruction and canalization). Thickened meninges are occasionally encountered in cases of syringomyelia. In such cases the thickened meninges compress the spinal vessels, with resulting softening of the cord. This and the absence of glial repair lead to cavity formation.

The accepted pathologic criteria of so-called syringomyelia, i.e., communication of the cavity with the central canal, ependymal lining of the cavity and gliosis, except for one small area, were not present in this case. The absence of evidence of an inflammatory process, the condition of the blood vessels in the compressed area, the thickened

dura, the accumulation of cerebrospinal fluid in the subarachnoid space (cases 1 and 3) and the pathologic changes in the compressed area of the cord with poor glial response are all in favor of a syringomyelia due to circulatory interference.

GENERAL COMMENT

That disintegration of intramedullary tumors may be the cause of cavity formation within the cord has been recognized by Schlesinger,[1] Westphal,[2] Kirch [3] and others. In this connection we wish to point out that traumatic necrosis as well as venous congestion in the spinal cord may also lead to the formation of cavities within it. Thomas and Hauser [4] and Alquier and Lhermitte [5] showed this to be true in caries. Lax,[6] Spiller,[7] Lloyd [8] and others described cases of trauma of the cord followed by symptoms of syringomyelia; at necropsy no traces of hemorrhage were found in the spinal cord. Schmauss,[9] in his experimental work on the production of cavities in the cord by trauma, showed that in these cases congenital predisposition may be of pathogenic significance. That hemorrhages in the spinal cord from injuries during birth may have a similar effect has also been pointed out by Schultze [10] and by Schlesinger.[1]

SUMMARY

Three cases of myelopathy presenting the clinical picture of so-called syringomyelia are described.

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1. In case 1 the myelopathy and syringomyelia were due to three factors: (1) destruction of the cord by an intramedullary tumor; (2) direct compression of the cord by thickened meninges and accumulated subarachnoid fluid, and (3) circulatory interference with the spinal cord vessels from the tumor and thickened meninges.

2. In case 2 the myelopathy and syringomyelia were due to destruction by (1) an intramedullary tumor, and (2) circulatory interference from the effects of a tumor on the intraspinal vessels of the cord.

3. In case 3 the myelopathy and syringomyelia were due to a tumor-like formation of the meninges and accumulated subarachnoid fluid compressing the cord and its vessels.

4. The myelin sheaths, axis-cylinders and anterior horn cells showed marked pathologic changes which could not be differentiated from those observed in the myelopathies from extramedullary compressions. In contrast to the marked myelopathies due to extramedullary neoplasm, the syringomyelic group showed a slight gliosis in two cases.

DISCUSSION

Dr. C. A. Mc Kendree, New York: What types of toxemia were included in the myelopathic cases?

Dr. M. Keschner, New York: The toxic cases in our series belonged to the ectodermal group, and the pathologic process resembled that produced experimentally by introducing various toxins into the circulation or into the subarachnoid space. In the absence of other demonstrable etiologic factors, we designated these cases as "toxic myelopathies."

Dr. T. J. Putnam, Boston: Do the authors feel that it is wholly justifiable to make a distinction between an inflammatory disease and a toxic disease on a purely morphologic basis?

Several years ago, I was able to produce, by the use of toxin, some lesions containing true inflammatory cells. They were lymphocytes and not scavenger cells, as was shown by the fat stains. The presence of infection in the tissue was fairly well excluded. Does Dr. Davison feel sure that the infectious agent was present in the case of myelitis which he presented?

Dr. W. G. Spiller, Philadelphia: That myelitis is a term which often is used carelessly has been recognized for a long time, and often the term neuritis is a misnomer. Should one speak of neuropathy instead of neuritis?

The finding of only two cases of myelitis in forty-three cases of diffuse nonsystemic disease of the cord confirms the opinion of its rarity. There has sometimes been a question as to what should be considered inflammation of the neuraxis. These authors offer as the criterion of inflammation the predominance of perivascular infiltration of lymphocytes, plasma and endothelial cells. They believe that the infection traveled up the posterior roots into the cord in one of their cases of myelitis, but they did not make the observations which were recently reported by Orr, who found the extramedullary portion of the posterior roots intact in purulent neuritis, while the intramedullary portion was degenerated.

It has been known for a long time that micro-organisms injected experimentally into the spinal fluid may soon disappear. In some cases of toxic myelopathy,

Keschner and Davison found the peripheral zones of the cord more degenerated, and they explain this as the effect of toxins in the cerebrospinal fluid. In my experience annular degeneration is rather rare, and the toxin explanation is the one usually employed.

The authors found sudden paraplegia in several of their cases of spinal syphilis. They ascribe the observations made in syphilitic patients chiefly to vascular disease, but I doubt whether all of the lesions in cases of spinal syphilis can be attributed to vascular occlusion. The spirochete has been found in the spinal cord in tabes.

I have seen degeneration of the spinal cord result from the passing of a bullet which did not disturb the outward conformation of the cord, and I, as they, attribute this condition to what is called concussion. There is a possibility of vascular injury in these cases.

Davison has not committed himself to the statement that subacute combined sclerosis of the cord never occurs from secondary anemia. The views regarding this question have changed in the past few years. I question whether congenital syringomyelia must communicate with the central canal. I have a section in which a small cavity lined with ependymal cells was found in the posterior septum apart from the central canal; this was evidently an embryologic defect.

The value of the paper of Drs. Davison and Keschner depends on the large number of cases studied and the convincing evidence that the number of cases of myelopathy far exceeds that of myelitis. As the authors state, the clinical diagnosis is often impossible. Do they suggest that we usually make the clinical diagnosis of myelopathy, which they say is most commonly caused by circulatory lesions; if not, what term is preferably to be used?

Dr. Nathaniel W. Winkelman, Philadelphia: The authors have given a rather broad and sweeping classification of the pathologic observations within the spinal cord. They have distinguished between inflammatory diseases, under which heading would be myelitis, encephalomyelitis disseminata, and anterior poliomyelitis, and degenerative processes which are classified as myelopathy. They have given a remarkable array of cases demonstrative of various conditions that may occur under these headings.

Dr. Eckel and I have been interested in tracing the vascular supply to the spinal cord; down to the fifth and sixth cervical segments the blood supply comes by way of the vertebral vessels, but from there down, the supply is through lateral branches which come from the deep cervical, thoracic, lumbar and sacral vessels. The original source of these lateral vessels is from the posterior wall of the aorta, the two vessels for each segment coming off at approximately the same level in close relation to one another. It is thus possible for a small lesion in the aorta, the result of a plaque, to occlude the stomas of both vessels to any particular segment of the cord, and in this way a sudden and complete softening of the cord can take place. Theoretically, while the three vessels in direct relation to the spinal cord may occlude simultaneously at any given level, practically this does not occur, and for this reason we have felt that a complete transverse myelomalacia is usually the result of the occlusion of the vessels as they come from the posterior wall of the aorta.

Dr. C. Davison: In answer to Dr. Putnam, we had only two cases of true myelitis. Perhaps we are mistaken, but a review of the literature convinces us that there are few cases of true myelitis that come to autopsy. The question naturally arises: How do we know whether we are dealing with a true case of myelitis or with one of myelopathy? When we have a section of the cord and the histopathologic process is distinctly inflammatory, without any evidence of a

myelopathic lesion such as that shown in the toxic group, we are inclined to call the process inflammatory. In the toxic group, for instance, there is a definite myelopathic process within the destroyed tissue without any evidence of reactive phenomena. In these cases in the absence of any inflammatory cells, we were inclined to disregard infection as the basis of the disease. It is true that inflammation is not always synonymous with infection, or vice versa. If the infectious process is of long duration, as in chronic encephalitis (parkinsonism), we may not find evidences of inflammatory cells in the nerve tissue. The duration of the disease undoubtedly plays an important rôle in the pathologic process. We are also aware of the fact that cases of true infection without any evidence of inflammatory cells have been described.

In answer to Dr. Spiller, for some time we recognized that the term neuritis is also a misnomer.

We agree with him that not all lesions in spinal syphilis can be attributed to vascular disease. We limited our problem to nonsystemic syphilitic disease of the cord, essentially those conditions which were due to occlusion of the spinal vessels; tabes dorsalis was not included in our series. In some of our cases there was slight evidence of invasion by the syphilitic process, especially at the periphery of the cord.

We fully agree with Dr. Spiller that in some cases congenital syringomyelia may not communicate with the central canal. We wished to stress, however, that in our cases the cavity was not lined by ependymal cells, and in the case in which some evidence of ependymal lining was found, it was due to the fusion of the cavity produced by the neoplasm with the original central canal. The ependymal lining belonged to the original lining of the central canal. It is obvious that our cases are not ones of congenital syringomyelia.

The difficulty of clinical diagnosis is emphasized in the paper. It is noteworthy that most of our cases were diagnosed clinically as myelitis by several groups of competent observers at various neurologic hospitals; at necropsy these cases proved to be myelopathies.

In answer to Dr. Winkelman's question, we have a few specimens in which the lesion was found exactly along the thrombosed vessel. The slide projected was not representative of all the cases we studied. We have some cases in which the posterolateral arteries presented only endarteritic and atherosclerotic changes. In these cases the myelopathic lesion was distributed in the region supplied by the vessel.

GROWTH OF A LOCALIZED FUNCTIONAL CENTER IN A RELATIVELY EQUIPOTENTIAL NERVOUS ORGAN

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In its early action the leg of the salamander can move only as the trunk moves. This means that the axial and appendicular muscles are a single consolidated and perfectly integrated system. When the appendage first moves independently of the axial muscles, its form of movement is the same as that which occurred earlier when it was wholly integrated with the axial muscles. This first local response of the leg is, therefore, the simplest form of the appendicular reflex. I am investigating the question: What does the nervous system do to give this movement a relative independence of the total action pattern and thereby give it local reflex function? The structural details of the nervous mechanism involved are still under investigation, but the general processes of growth of that part of the spinal cord which is related to the appendage have been studied exhaustively, and this report deals only with that phase of the problem.

In all problems relating to the growth of the nervous system it must be kept constantly in mind that proliferation of cells and differentiation of cells are very different processes. In the nervous system they operate differently in time and in space, and it has been shown that in metabolism they differ qualitatively. In a broad way this difference is illustrated by the well known circumstance that mitosis ceases very early in the development of the human brain, whereas differentiation of cells continues far on into the life time of the individual. This principle can also be observed in detail in the early phase of development of the central nervous system of the lower vertebrates. All studies on hyperplasia in the nervous system, therefore, should determine and specify whether it is proliferation or differentiation, or both processes that are concerned; and the same distinction should be made in all studies of the normal growth of the nervous system.

The proliferation of cells may be studied by two procedures: by determining the numbers of cells that are in mitosis at given times in particular regions, and by determining the total numbers of cells at

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different stages during growth. These procedures, however, have different meanings. The number of cells that are in mitosis at a given time indicates the speed at which proliferation was going on at the moment of death of the tissue; the increase in the numbers of cells over a given period tells the rate of proliferation during that period. Both procedures have been followed in this investigation. Also, the relative volumes of the gray substance and of the white substance have been determined.

DEVELOPMENT OF MOTION AND OF REFLEX RESPONSE

The study covers ten stages in the development of the salamander, ranging from two days after swimming began up to and including the stage in which local reflexes of the leg first occur; it includes the tenth to the twentieth spinal segments inclusive. The segments which eventually innervate the leg are the sixteenth, seventeenth and eighteenth.

When it begins to function, the spinal cord of Amblystoma, excepting in its most anterior part, is virtually equipotential along its longitudinal axis, for all segments are doing the same thing: They are conducting impulses headward and tailward and are giving out motor and sensory nerves of the same order. In the earliest stages involved in this study, the same equipotentiality prevails in that part of the cord which is under consideration, namely, the tenth to the twentieth segments inclusive.

In the early growth of the spinal cord of the region investigated, mitotic figures occur in numerous, irregularly distributed, restricted foci. These foci are obviously transitory, for they are found in various locations in different specimens. They represent localized regions of acceleration of proliferation. They are rarely found to be bilaterally symmetrical in their arrangement, and they hold no definite or constant relation to the motor or sensory nerve roots. Accordingly, proliferation as indicated by mitosis appears to be unorganized. In reality, however, it is definitely organized, for when the numbers of cells in each segment are charted on the longitudinal axis of the spinal cord, the graph so derived conforms to a definite and constant pattern. A graph representing the numbers of cells in successive segments of the spinal cord falls gradually and with striking evenness as compared with similar graphs representing the numbers of mitotic figures. The latter graphs are exceedingly choppy from segment to segment. Nevertheless, the net result of mitosis over a given period conforms to a definite pattern of growth in the region of the cord concerned. Individual parts may grow differently from moment to moment, apparently haphazardly, but they are regulated in such a way that they produce a definite and constant result. There is obviously a compensatory regulation of parts by a dynamic pattern of the whole.

This regular pattern of growth by proliferation of cells changes greatly at about the time the leg appears on the surface of the body. As indicated by mitosis, the speed of proliferation is accelerated from the fourteenth to the eighteenth segment inclusive as compared with the segments in front of and behind these segments. This region is much more extensive than the three segments that are destined to innervate the leg and lies much more in front of those segments than behind them. A graph charted now according to numbers of dividing cells in the several segments of the cord has a high peak in the seventeenth segment, which is the center of the region that is destined to innervate the leg; this peak is approached evenly from the direction of the head and from that of the tail, but much more gradually from that of the head. A similar, but less marked, peak of the graph representing the numbers of cells in the successive segments also occurs at this time, but it lies in the sixteenth instead of in the seventeenth segment. Obviously, therefore, there has been acceleration of proliferation in this region of the cord for an appreciable length of time before the leg has reached the stage of clear definition on the surface of the body.

At a slightly later stage the peak of the graph of cell numbers comes to lie in the seventeenth segment along with that of mitosis. But immediately following this, the peak in the graph of mitosis in the leg level disappears, and this graph again becomes choppy and runs at a lower level. This occurs at the time at which the leg first moves as a part of the total pattern and is without reflex response. But as the leg acquires reflex response another peak appears in the graph of mitosis, approximately at the leg level. The first period of acceleration obviously has to do with the development of the movement of the leg as a whole; the second is probably concerned with the development of movement in the distal parts of the leg and foot.

At the time at which the graph for numbers of cells in the successive segments rises from the thirteenth to the sixteenth segment and then falls rapidly to the eighteenth, the graph for cross-section area of the gray substance rises and falls within the same segments and, like the graph for numbers of cells, reaches its peak in the sixteenth segment.

Differentiation, however, does not yet express itself in local acceleration of the formation of nerve fibers, for the graph for areas of cross-section of the white substance falls evenly from the thirteenth to the eighteenth segments. There is, therefore, in this stage, no correlation between the acceleration of proliferation or differentiation and the ingrowth of fibers from the more rostral parts of the cord. If such a correlation existed, the graph for the white substance would be higher in the region of acceleration of growth of the gray substance. But this is not the case.

The relatively even descent of the graph for the white substance from the thirteenth to the eighteenth segment persists until the stage in which the leg begins to move with the trunk as a total pattern. At this time the graph for the white substance maintains a relatively high level from the tenth to the seventeenth segment, from which point it falls rapidly tailward. This high level of the graph for the white substance is apparently due to the ingrowth of the dorsal nerve roots, the fibers of which grow more headward than tailward. But it is not correlated in time with the initial acceleration in division of cells, for this acceleration occurred at a much earlier period. Meanwhile the peaks of the graphs for the gray substance and for the numbers of cells have come to lie in the seventeenth segment, which is the middle one of the three that innervate the leg. Here, then, a localized acceleration of growth in a functional nervous unit gives rise to a localized functional center of nervous action. Is this true, also, for higher centers?

COMMENT

Tilney and Kubie [1] reported that the wall of the vesicle of the end-brain or cerebral hemisphere of the 5 mm. embryo of the cat consists of a single layer of ependyma. In the embryo of 9 mm., covering the ependyma is another layer which is the forerunner of the mantle and marginal layers of His. This layer is thickest over the lateral surface of the hemisphere and gradually thins out over the ventral surface toward the median line. Tilney and Kubie called this an ichthyopsid stage of development. In the embryo of 10 mm. there is extensive migration of cells from the ependymal layer into the mantle zone. This is the beginning of the three-layered stage of the cortex. There are now ependymal, mantle and marginal zones. In a 12.5 mm. embryo, the three layer condition extends over the whole hemisphere. A fourth layer makes its appearance in the 13.0 mm. embryo. This layer occurs in the lateral wall of the vesicle "about midway between the two poles and extends upward from the junction of the ventral and lateral surfaces about half-way to the dorsal surface." In this the primordial granular layer makes its appearance. "It is limited to a small area on the lateral surface of the brain wall." It is differentiated into a suprastriatal and a juxtastriatal division. These differ strikingly in their cellular organization. This is the beginning of the differentiation between the paleocortex and the neocortex. In the 14 mm. embryo the fourth layer of the cortex is present in somewhat less than a quarter of the entire wall of the vesicle. The more central regions of this layer have the greatest thickness. Of a 29.5 mm. embryo, Tilney and Kubie said: "The area

1. Tilney, Frederick, and Kubie, Lawrence S.: Bull. Neurol. Inst. New York **1**:229 (June) 1931.

of the bulbus olfactorius is notable for two reasons: (1) a definite granular layer invests its cephalic portion, and (2) a relatively wide band of more primitive brain wall intervenes between this granular differentiation and the granular layer covering the rest of the cerebral hemisphere." In an embryo of 50 mm. a striking development takes place in the lateral wall of the hemisphere in the form of a secondary lamination. This is limited to less than one fifth of the entire lateral area of the hemisphere. This lamination is extended still further in the 60 mm. embryo.

The lateral wall of the end-brain of the cat is, therefore, the locus of accelerated growth and of differentiation in regard to the primitive mantle, marginal and granular layers; while a second locus of acceleration of differentiation in the olfactory lobes gives rise to a granular layer that is separated from that of the hemisphere by an area of more embryonic tissue. In this early phase of development the cortex of the cat, therefore, follows the plan of growth of the lowest order of localized functional centers in the spinal cord of Amblystoma.

In exploring the cerebral cortex of new-born kittens with electrodes, Langworthy [2] found that the only region from which response could be elicited was the region of the cruciate sulcus. Langworthy said that in this center maturation "appears to begin on the surface of the gyri, gradually progressing toward the sulcus. . . . The cells lying in the depths of and on the anterior and posterior walls of the sulcus are the last to mature, and throughout life this portion of the motor cortex appears less differentiated than the areas upon the surface." This picture of progressively advancing differentiation from the margins of a localized functional region to its center supplements the description of Tilney and Kubie, and confirms the conclusion that I draw from their report.

Bolton and Moyes [3] found that in the 18 cm. human fetus, considerable progress has already been made in the specialization of cortical areas; the precentral and postcentral cortices are "remarkably well evolved in comparison with the rest of the cortex," the Betz cell area can be mapped out accurately, the visuosensory area can be defined with accuracy, the cingulate cortex is relatively advanced in development, but the anterior frontal cortex is extremely embryonic. This is clear evidence that localized functional centers in the cerebral cortex of man are clearly defined in a very early period, and that they are separated by areas of less differentiation, just as in its early development, the leg center of the spinal cord in Amblystoma is separated from the center of the forelimb by a region of low degree of differentiation. Accordingly, localized functional centers of the cerebral cortex of the cat and

2. Langworthy, O. R.: Contrib. Embryol. (no. 104) **19**:177, 1927.

3. Bolton, J. S., and Moyes, J. M.: Brain **35**:1, 1912.

of man appear to develop in the same manner as such a center arises in the spinal cord of Amblystoma, namely, by acceleration of differentiation within a relatively equipotential system.

SUMMARY

The point of chief interest in the growth of this localized functional nerve center is that structural development agrees in principle with the development of behavior. Just as local reflex action emerges within an integrated total pattern, so the center of control of local reaction develops within the mechanism which, as a relatively equipotential system, integrates the total pattern. Local functional centers are not added by accretion to an already functioning mechanism, but they grow up within that mechanism and are normally held under its control.

ALCOHOL INJECTED INTRAVENOUSLY

ITS PENETRATION INTO THE CEREBROSPINAL FLUID IN MAN

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AND
HENRY W. NEWMAN, M.D.
SAN FRANCISCO

As early as 1900, Nicloux [1] found that in dogs about an hour after the ingestion of a single dose of alcohol the values in the blood and the spinal fluid were approximately equal. In 1913, Schumm and Fleischmann [2] administered a constant dose of alcohol to a series of patients, puncturing each patient at a different interval after ingestion and thereby obtaining a composite curve for the alcohol in the blood and in the spinal fluid. They found that during the first hour the alcohol in the blood rose more rapidly than that in the spinal fluid, but that during the decline of the alcohol in the blood the alcohol in the spinal fluid surpassed it and remained at a higher level. Because of Schumm and Fleischmann's use of single punctures for various patients, some of their figures fall far out of line. Recently, Abramson and Linde [3] repeated the work, using a dose of alcohol proportional to body weight and leaving the lumbar needle in place during the three hours in which they collected the specimens. They showed that the alcohol content of the spinal fluid rises more slowly than that of the blood and reaches its maximum later. This maximum is lower than that reached by the blood. During the period of decline, the alcohol in the spinal fluid remains higher than that in the blood. Gettler and Freireich [4] showed, in a fairly large series of patients brought to the hospital when intoxicated, that the alcohol content of the spinal fluid was almost invariably higher than that of the blood. This is in accord with our experience. The following problem then presents itself: In these cases, is the fact that the alcohol level of the spinal fluid is higher than that in the blood due to an active secretion of alcohol into the spinal fluid, or can the explanation be wholly that in all the cases the fluids were obtained

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From the Division of Neuropsychiatry, Stanford University Medical School.

Read by title at the Fifty-Ninth Annual Meeting of the American Neurological Association, Washington, D. C., May 9, 1933.

1. Nicloux, M.: Compt. rend. Soc. de biol. **52**:620, 1900.

2. Schumm, O., and Fleischmann, R.: Deutsche Ztschr. f. Nervenh. **46**:275, 1913.

3. Abramson, L., and Linde, P.: Arch. internat. de pharmacodyn. et de thérap. **39**:325, 1930.

4. Gettler, A. O., and Freireich, A. W.: J. Biol. Chem. **92**:199, 1931.

some time after the imbibition of alcohol, when the alcohol in the blood was in the period of decline, during which we know it to be surpassed by that of the spinal fluid? The present work is an endeavor to determine this point.

TECHNIC

Alcohol may be administered to man in a number of ways. The oral route is certainly the simplest, and it is the traditional method. For the present work it has the disadvantage of irregularity of speed of absorption from the gastrointestinal tract, with attendant inability to control accurately and rapidly the alcoholic concentration in the blood. Rectal injection partakes of the same disadvantages and is irritating. Any concentration compatible with adequate dosage would be too irritating for subcutaneous injection. The intraperitoneal injection of a 33 per cent solution has been employed for anesthesia, but would[5] be ill-adapted to experimental work. There remains the intravenous route, which has been extensively employed[6] for anesthesia during the past few years.

We chose this method because of several important advantages. The dosage can be controlled to a nicety, as can the rate of administration. The factor of absorption is eliminated. Less important in this work than in the appraisal of the psychologic effect of alcohol is the fact that the subject need not be aware that he is receiving alcohol, an end which is impossible of achievement with oral administration.

As an intravenous anesthetic, various concentrations of alcohol in a number of vehicles have been employed. Generally it is accepted that the concentration should not exceed 40 per cent and the rate of injection 40 cc. per minute. The dose required for surgical anesthesia varies from 2 to 3 cc. per kilogram of body weight. The dangers of the method lie in the injurious action of the alcohol on the red blood cells, giving rise to hemolysis and agglutination. We endeavored to minimize this danger by reducing the strength of the solution and the speed of injection, as well as by reducing the dose from that reported to be safe for anesthesia.

As a routine we have employed a solution of 25 per cent alcohol in a physiologic solution of sodium chloride injected at a rate not to exceed 10 cc. per minute. The dose generally employed was 1 cc. per kilogram. We have made over seventy-five injections by this method, without doing perceptible harm to the subject except occasionally to cause thrombosis at the site of the injection. In a number of cases in which the urine was tested for red cells and hemoglobin none was found.

Interestingly enough, instead of showing the boisterousness usually associated with intoxication, a large percentage of the subjects became tearful, while a number slept through the whole procedure. A great difference in reaction to the same dose of alcohol among different patients was evidenced. We hope in the future to be able to correlate this variation with the type of subject.

In four cases there was emesis about an hour after the injection, suggesting that the rather common emesis from imbibed alcohol may be due to central action rather than to gastric irritation, since we have shown the concentration of alcohol in the stomach after intravenous administration to be exceedingly low.[7]

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5. Thursz, D.: Wien. klin. Wchnschr. **43**:1284, 1930.

6. Garcia, Miguel: Mexico City, Mexico, E. Mesones Imp., 1929. Constantin, J. D.: Lancet **1**:1247, 1929; **1**:1393, 1930. Fohl, T.: Arch. f. klin. Chir. **165**: 641, 1931. Nitzescu: Compt. rend. Soc. de biol. **104**:25, 1930.

7. Newman, H. W., and Mehrtens, H. G.: Proc. Soc. Exper. Biol. & Med. **29**:145, 1932.

The determinations for alcohol were carried out according to the method of Cannan and Sulzer,[8] which depends on the distillation of the fluid in vacuo at a temperature of from 40 to 50 C. and the passage of the vapor through a solution of potassium dichromate in strong sulphuric acid. The amount of potassium dichromate required to oxidize the alcohol is determined by titration with sodium thiosulphate after the addition of an excess of potassium iodide, starch being used as the indicator. All of the determinations were made by one of us with the same apparatus, so that errors due to variations of technic were eliminated.

It has been remarked by many workers in this field that[9] there is normally present in the body fluids a certain amount of a volatile oxidizable substance. This may or may not be alcohol, as the methods of quantitative analysis are not specific. In our experience, the values varied from 2 to 5 mg. per hundred cubic centimeters, which is in accord with the findings of others. In order to eliminate this factor, we invariably tested the fluid before the injection of alcohol was made, so that our figures represent the increase in alcohol over the value normally present in each subject.

It has also been shown that the plasma contains more alcohol than do the red cells.[10] Since the red cells do not take part in any process of diffusion, it is evident that the amount of alcohol in the plasma and not that in the whole blood is the important factor. We verified this discrepancy between whole blood and plasma, which amounts to between 10 and 15 per cent. In all cases in which the maximum values of alcohol in the blood and in the spinal fluid were compared, the determinations were made on plasma rather than on whole blood.

RESULTS OF EXPERIMENTS

A single dose of 1 cc. per kilogram of body weight was administered to a number of subjects, and the level of the alcohol in the blood during and after the injection was followed. A typical curve is seen in chart 1. It will be seen that, as would be expected, the maximum was reached at the end of the injection. The decline was at first rapid, but gradually decelerated until a nearly constant rate was achieved. We believe that the initial sharp decline was due to rapid diffusion of the alcohol from the blood into the tissues. When the tissues became saturated, the further slow decline was accounted for by elimination of the alcohol, which was largely by oxidation. At the end of eight hours, the alcohol had practically disappeared from the blood stream. We noted a considerable variation in the maximum height to which the alcoholic content of the blood rose in various persons receiving the same dose per kilogram of body weight, which has led us to the supposition that the amount of active protoplasm, rather than the body weight, determines the capacity for alcohol. This correlates well with the finding that the amount in bone and fat is small.[11]

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8. Cannan, R. K., and Sulzer, R.: Heart **11**:148, 1924.
9. Gettler, A. O., and Tiber, A.: The Alcoholic Content of the Human Brain, Arch. Path. **3**:218 (Feb.) 1927.
10. Miles, W. R., Jr.: J. Pharmacol. & Exper. Therap. **20**:265, 1922.
11. Smith, G., and Stewart, C. P.: Brit. M. J. **1**:89, 1932.

It was found that the alcohol in the blood could be maintained at a fairly constant level over a period of hours by the use of a continuous intravenous drip of alcohol following the first injection, as shown in chart 4. Here the initial dose of 1 cc. per kilogram was given more slowly, 5 cc. of 25 per cent alcohol per minute, in order that diffusion through the tissues might keep pace with the injection. The subsequent maintenance dosage was found to be 0.2 cc. per kilogram per hour, given as a 10 per cent solution for convenience in regulating the flow. We intend to use this method further for determining the rate of oxidation of alcohol when the alcohol in the blood is at varying con-

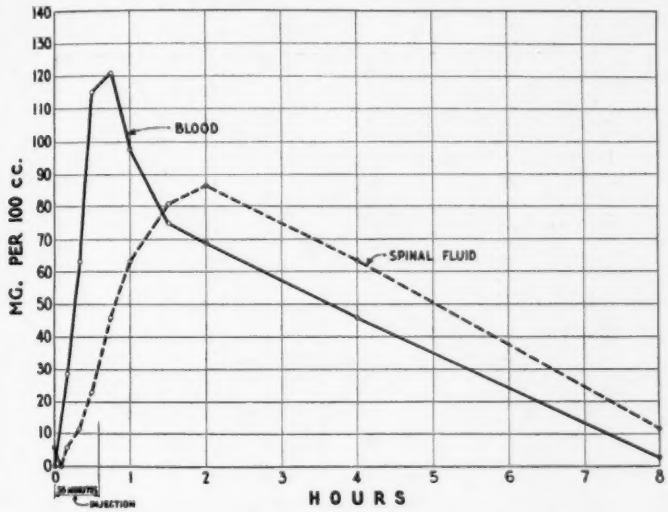

Chart 1.—The curves for alcohol in the blood and in the lumbar spinal fluid on a single injection of 1 cc. of 95 per cent alcohol per kilogram of body weight.

centrations, and to determine accurately the difference in rate of oxidation in habituated persons and in abstainers.

Chart 1 also shows the curve of the alcohol level of the spinal fluid obtained by lumbar puncture following a single injection. It will be noted that it rises slowly, attains the height of the diminishing alcohol level of the blood in about eighty minutes, reaches a maximum less than that of the blood and during the period of decline remains higher than that of the blood. This confirms the work of Abramson and Linde. In a series of seven subjects so treated, the curves for the alcohol levels of the blood and the lumbar fluid crossed between eighty and one hundred and twenty minutes after the injection. Interestingly enough, if one subscribes to the theory commonly held, that the spinal fluid is the best index of inebriation, the signs of drunkenness in no

way showed the lag that one might expect from the slow rise in the alcohol level of the lumbar fluid. In our considerable experience the subject was invariably more intoxicated, judging from his actions and subjective sensations, at the end of the injection, when the alcohol of the blood was at its maximum and that of the lumbar fluid was negligible, than at any subsequent time. Thus, during the first hour after the imbibition of alcohol the lumbar fluid is a poor index of intoxication.[12]

Our next step was to follow the alcoholic content of the spinal fluid obtained by cisternal puncture. The results appear in chart 2. It is striking that the curve for the cisternal fluid closely follows that

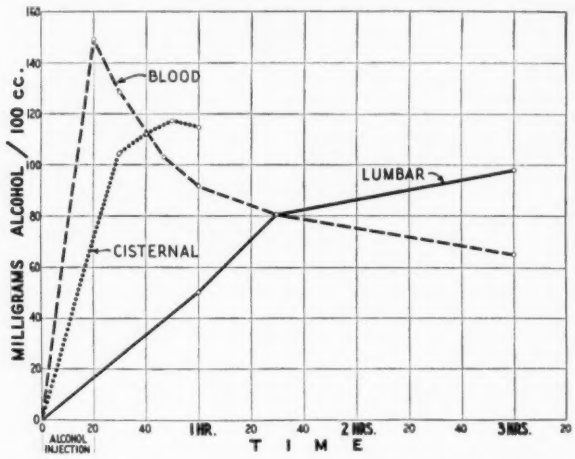

Chart 2.—Alcoholic content of the cisternal spinal fluid contrasted with that of the blood and of the lumbar spinal fluid. One cubic centimeter of alcohol per kilogram of body weight was injected.

for the blood, while that for the lumbar fluid shows its characteristic lag. Thus it is seen that alcohol appears more promptly in higher concentration in the cisternal than in the lumbar spinal fluid. As a patient was available who showed in the upper thoracic region a spinal subarachnoid block which was revealed by iodized poppy seed oil, 40 per cent, and which was subsequently proved at operation to be a circumscribed pachymeningitis, we repeated the experiment on her. The results are shown in chart 3. The curve for the cisternal fluid followed the usual form, but that for the lumbar fluid showed an abnormally long delay, crossing the blood curve one hundred and eighty minutes after the injection, as against the normal range of from eighty to one hundred

12. Newman, H. W., and Mehrtens, H. G.: Proc. Soc. Exper. Biol. & Med. **30**:725 (March) 1933.

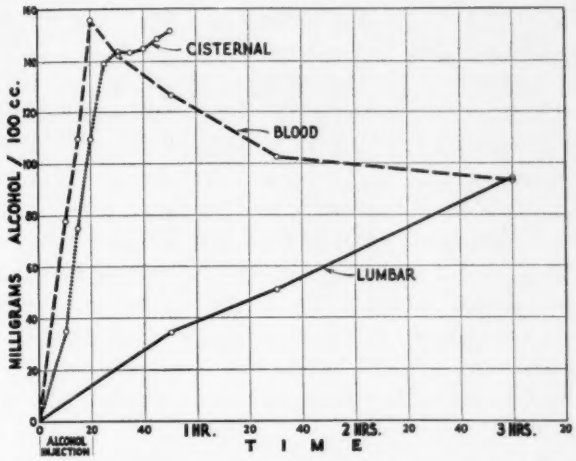

Chart 3.—The alcoholic content of the blood and of the spinal fluid in a patient with spinal subarachnoid block in the upper thoracic region. One cubic centimeter of alcohol per kilogram of body weight was injected.

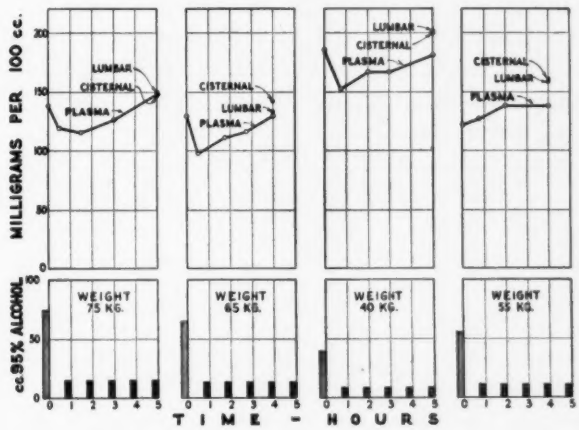

Chart 4.—The alcohol levels in the blood plasma and spinal fluid in four patients in whom the alcohol content of the blood was maintained from four to five hours by the intravenous drip method. The shaded columns indicate the initial injection; the solid, the continuous injection of 0.2 cc. per kilogram of body weight each hour.

and twenty minutes. From this we conclude that at least most of the alcohol finds its way into the fluid in the cephalic end of the system, which fits in well with the theory that the fluid is formed largely in the ventricles by the choroid plexuses.[13]

By the intravenous drip method we then maintained the alcohol in the blood at a practically constant level for a period of from four to five hours in a series of four patients. At the end of the period, cisternal and lumbar punctures were made, and the alcoholic content of the specimens of fluid was compared with that of simultaneously obtained blood plasma. As will be seen in chart 4, in three of the four patients the values for spinal fluid were significantly higher than those for the blood plasma, while in the fourth patient they were approximately equal. Any period of decline in the alcoholic content of the blood was eliminated by the experimental conditions, yet the alcohol in the spinal fluid remained in excess of that in the blood in the majority of cases.

COMMENT

The evidence which we have presented seems to indicate that alcohol enters the cerebrospinal fluid predominantly in the cephalic end of the system, since, after intravenous injection there is a much more rapid rise in alcohol content in the fluid obtained by cisternal puncture than in that obtained by lumbar puncture. This lag of the lumbar curve is augmented still further by the interposition of a subarachnoid block between the cisternal and the lumbar spaces. The fact that in three of four cases in which the alcohol in the blood was kept at a constant level the alcohol in the spinal fluid ultimately exceeded the maximum in the blood plasma raises the question as to whether there is an active secretion of alcohol to account for this excess. The excess of alcohol in the spinal fluid over that in the blood in inebriated subjects is well known,[4] but it can conceivably be accounted for by the fact that punctures are usually made some time after the alcohol is imbibed, so that the alcohol in the blood is on the decline, and the lag of the decline in the alcohol of the spinal fluid, as shown by Abramson and Linde and us, comes into play. No such situation existed in our experimental work, however, in which by maintaining the alcohol in the blood constant we eliminated this period of decline, yet in the majority of cases the alcohol in the spinal fluid remained higher than that in the blood plasma. On first impression, it seems inevitable that a secretory function must be invoked, since by simple diffusion it is impossible to achieve a higher concentration on one side of the membrane than exists

13. Weed, L. H.: J. M. Research **26**:93, 1914. Levinson, A.: Cerebrospinal Fluid in Health and in Disease, ed. 2, St. Louis, C. V. Mosby Company, 1923, p. 46.

on the other. However, to consider the excretion of urea by the kidney: The glomerular filtrate [14] is a protein-free filtrate, containing urea in concentration equal to that in the blood. However, as it flows through the tubule the water is in part absorbed, and the result is a great increase in the concentration of the urea. Can one not visualize an analogous situation applicable to our problem, with the formation of a fluid, largely in the ventricles, which contains alcohol in equilibrium with that in the blood plasma, but which on passing out into the subarachnoid space is absorbed more rapidly than is the alcohol, with a resulting concentration of the alcohol in the spinal fluid? It has been shown that there is an individual variation in the permeability of the meninges to other substances [15] which may account for the varying degree of concentration in the four subjects examined.

In spite of the attractiveness of the aforementioned theory, active secretion of the alcohol by the choroid plexus remains a possibility that cannot be ruled out in the light of present knowledge. The problem may finally be settled by the employment of ventricular puncture.

SUMMARY

1. The intravenous administration of alcohol is admirably adapted to the study of the psychologic effects of alcohol on man.

2. After a single dose of alcohol is administered intravenously, the alcohol in the lumbar spinal fluid rises much more slowly than that in the blood, attains its maximum later and declines more slowly. The alcohol in the cisternal fluid rises promptly and closely approximates that in the blood.

3. When the alcohol in the blood is kept at a constant level for from four to five hours, the alcoholic content of the lumbar and cisternal fluids at the end of this time is equal to, or in excess of, that in the blood plasma.

4. The evidence from this work seems to indicate that alcohol enters the spinal fluid by diffusion from the blood, probably largely from the choroid plexuses. The higher alcohol content of the spinal fluid as compared with that of the blood plasma may be due to a relative impermeability of the absorbing system to alcohol, with a resulting concentration of the alcohol, or to an active secretion of the alcohol by the choroid plexus. We favor the former hypothesis.

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14. Macleod, J. J. R.: Physiology and Biochemistry in Modern Medicine, ed. 5, St. Louis, C. V. Mosby Company, 1930, p. 758.

15. Mehrtens, H. G., and West, H. F.: The Absorption of Phenolsulphonphthalein from the Subarachnoid Space in Diseases of the Central Nervous System, Arch. Int. Med. **20**:575 (Oct.) 1917.

Clinical Notes

ASTROCYTOMA OF THE CEREBELLUM

Survival Period of Forty-Five Years Without Operation

LOUIS HAUSMAN, M.D., AND LEWIS STEVENSON, M.D., NEW YORK

The duration of this case of tumor of the brain, in which no surgical intervention was attempted, covered approximately forty-five years, to our knowledge the longest survival period on record. Despite the protracted course of the disease, the patient, even at a very late date, presented few neurologic signs and for the most part was comfortable, alert and able to attend to business duties. The first symptoms appeared between the ages of 6 and 8 years; the patient died at the age of 53. Postmortem examination revealed an astrocytoma of the cerebellum.

In view of the importance which attaches to the record, it is presented in detail. Fortunately, at the age of 16, thirty-seven years before the fatal termination of the illness, the patient consulted Dr. Allen Starr, who with his usual clinical acumen made a diagnosis of tumor of the brain and published a report of the case in the *Medical Record,* in 1896. This record is incorporated in the history and incidentally serves to indicate the great strides that have been made in the concept of, and in the therapeutic approach to, the problem of cerebellar cysts.

REPORT OF A CASE

Anamnesis.—The anamnesis was obtained from the patient and supplemented by his wife, his sisters and a brother, all intelligent and dependable.

Mr. W. was born on Feb. 15, 1879, and died on Aug. 29, 1932, at the age of 53. The family history revealed no pertinent facts. The mother died at the age of 78 of "apoplexy" following two previous attacks. The father's death, at the age of 79, was ascribed by the family to senility. The patient was the third of eight children. There is no history of familial disease or of syphilis. Two children died of pneumonia. Four sisters and one brother were living and well.

Although the patient was born with a large head, birth was normal. He had measles as a child but otherwise was described as healthy until between 6 and 8 years of age, when he had an attack of "sunstroke." This occurred one day in summer, when he complained of an unusually severe headache; his apathy on this occasion was particularly noticeable because he failed to run out with the other children to greet his mother who was returning from a holiday after an absence of several months. The onset was sudden; he became nauseated and vomited. The family was alarmed and consulted Dr. Seguin and Dr. Delafield. These eminent physicians, it is said, attributed the condition to "stomach trouble" and

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From the neurologic service of Dr. Foster Kennedy, Second Medical Division of Bellevue Hospital.

Read at the Fifty-Ninth annual meeting of the American Neurological Association, Washington, D. C., May 10, 1933.

instituted gastric lavage when the patient found it difficult to retain food. A sister remembered that the patient was asked to walk a chalk line, which he was unable to do because he "staggered so much." When he walked he veered to the right. During this period the family lived outside New York and had to take a ferry-boat when they went to visit the physicians. It was recalled that the patient stumbled so much during the crossing that the mother had to hold him by the hand.

Sometime in this period he was seen by Dr. Story, of Flushing, N. Y., who suspected a tumor of the brain. The patient remained in bed for three years. Between the ages of 12 and 14 years, he fell off a high bicycle and struck his head; he was not unconscious and except for severe headaches apparently had no unpleasant results from the accident, which was considered trivial, although it is recalled that the mother noticed then that the "right side of the face was a little thinner." At the age of 16 years, the headaches again became severe and annoying. The patient was able to play baseball, but he saw double and vision in the right eye became poor. Dr. Allen Starr saw the patient at this time and, because of the interesting problem which the case presented, reported his observations under the title, "A Contribution to Brain Surgery, with Special Reference to Brain Tumors." [1]

"The patient was a boy, sixteen years of age, of perfectly healthy parents, there being no direct or indirect history of syphilis in either parent, and the boy himself presenting no evidence, direct or indirect, of having had the disease. In March, 1895, he began to suffer from a disturbance of his eyesight, and it was noticed that his eyes had a peculiar appearance. He was taken to a certain specialist in New York, who immediately discovered muscular insufficiency and divided the internal recti without any relief. Two weeks later he began to suffer from very intense headaches, vomiting, and marked mental dulness, and it was noticed on every occasion that he staggered slightly in walking. Lateral oscillation of the eyeballs was then noticed, and his headaches, which increased in intensity, interfered with his sleep at night. On April 24th, when I first saw him in consultation with Dr. Story of Flushing, L. I., the boy was very ill. He was confined to bed and any motion increased the intense headache from which he constantly suffered. He was extremely emaciated, and frequent vomiting was attended by great vertigo and prostration. His eyes were prominent, his pupils were dilated, there was a slight deviation of the left eye outward, he saw double, vision was reduced two-thirds, and there was very marked nystagmus on any lateral movement of the eyes. Examination by the ophthalmoscope revealed a double optic neuritis, with great distention of the veins but without hemorrhages in the retina. There was no paralysis of the face, but he complained of numbness in the left side of the face and some weakness in the muscles of mastication on the left side of the jaw. His tongue deviated to the left. There were no paralysis or ataxia of the hands and no disturbances of sensation in the extremities or body. There was no paralysis or ataxia of the legs when at rest, and his knee jerks were normal. There was no clonus. On standing up, his head fell forward, but he was able to straighten it with some effort, holding it, however, somewhat forward and toward the left. He staggered painfully in standing and in walking, so that he was unable to walk without assistance. The staggering was of the type recognized as cerebellar. There was considerable ringing in the left ear, but his hearing was the same on both sides. He had had on three occasions retention of urine which had to be relieved by a catheter, and he was extremely constipated.

1. Starr, A.: M. Rec. **1**:146, 1896.

"With these general symptoms of brain tumor, and with the local symptoms of cerebellar disease, together with an affection of the fifth, eighth, and twelfth nerves on the left side, it seemed evident that this boy must have a tumor, involving the cerebellum and producing compression of the left side of the cerebral axis; a tumor, in a word, whose position was such as to make any operation absolutely impossible. In the absence of any history of syphilis it seemed proper to give an absolutely unfavorable prognosis, and yet to resort to inunctions and large doses of iodide as affording the only possible hope. These were immediately begun and the iodide rapidly run up to two hundred and fifty grains a day. A steady improvement began in about two weeks after the treatment was instituted, and by June 15th he was up and about, without headaches, without vomiting, and walking without assistance quite well. He still staggered slightly, however, with a tendency to go toward the left; his tongue still deviated to the left. The left side of his face was still hyperaesthetic and at times painful. His eyesight improved and the optic neuritis was subsiding. The improvement went on during the entire summer, and at present the boy is quite well, with the exception of nystagmus and a slight right facial paralysis which has developed slowly. The appearance of his eyes is such as to suggest the previous existence of a neuritis, though his sight is normal. He is still taking two drachms of the iodide of potassium daily.

"This case then shows that even in some individuals where there is no history of syphilis medical treatment for a brain tumor occasionally succeeds. Whether this treatment may be aided by diminution of the intracranial pressure may be left an open question."

Course.—From 1896 to 1920 the patient was well except for an attack of scarlet fever at the age of 16 years and a vague history of tuberculosis at the age of 20, described as a "delicate throat," for the treatment of which he went west and remained there two or three years. We were informed by members of the family that the diagnosis of tuberculosis was at no time definitely established.

In 1920, at the age of 41, the patient married. At the time of his death, his wife and two children, aged 12 and 10 respectively, were living and well, except for the oldest child who had a marked hypothyroidism and recently had been subject to mild episodes of petit mal. There was no history of miscarriages or stillbirths in the family. The wife stated that when she married the patient twelve years before, he appeared to be in good health. Up to the last few months of his illness he was bright, keen, alert and quick in repartee, and displayed a good sense of humor and a good memory. At the time of marriage he was well physically, although the wife recalled that when they danced together his balancing was not good and he had a tendency to reel to the right, so that she had to hold him when the dance stopped. He always complained of poor eyesight.

Several years after marriage he began to complain again of severe headaches, localized at the back of the head, which became so troublesome that Dr. Starr was again consulted. Potassium iodide was again administered, but without success. Inunctions of mild mercurial ointment, however, gave some relief. The patient was susceptible to "head colds," which were usually followed by severe headaches. At one time an otolaryngologist relieved the headaches considerably by nasal instillations of mild silver protein.

Dr. Starr kept the patient under observation. In 1924, the condition became so serious that surgical intervention was considered. But again the administration of mercury and potassium iodide proved so efficacious that the idea of operation was abandoned, and likewise the diagnosis of a tumor of the brain, and Dr. Starr became more and more reconciled to the belief that the underlying process was syphilitic.

On Dec. 31, 1925, and thereafter the patient was examined by Dr. Scott also. He was then 46 years old. His complaint was frontal headache for one week. Dr. Scott reported: "The eyes had been examined two months previously and were pronounced normal. Physical examination gave negative results except for sluggish pupils; the kneejerks were active and equal; there was no disturbance of equilibrium. The blood pressure was 110 systolic and 80 diastolic. The headache cleared up after medication with coal tar and colon irrigations."

The patient felt well until 1927. On January 24 of that year he reported for an ophthalmologic examination to Dr. Ward Holden, who found: "Right corneal sensibility was diminished. The pupils were 3 mm. in diameter, round, and with good reaction. There were diplopia on looking to the right and up and coarse nystagmus on looking to the right. Vision with glasses was 20/30 in the right eye and 20/15 in the left. The limits of the visual fields were normal. In the right eye there was a small paracentral scotoma to the right of the fixation point. The fundi were normal. The diminished vision was thought to date from the first attack or possibly from birth. There was possibly reduced hearing in the right ear."

The patient was subsequently observed by Dr. Scott. The following reports are of interest: "May 24, 1927. The right eyeground showed a pale disk and no hemorrhage or edema; the left was normal. There was no headache or dizziness. March 28, 1930: The patient was treated for an acute upper respiratory infection. There were no symptoms referable to the central nervous system."

Recent Illness.—Until about two years before death, the patient was fairly well and active, except for the irregular recurrence of occipital headaches. He continued to go to his place of business. About October, 1930, the gait gradually became more unsteady and memory defective. He would leave in the morning to go to the bank and disappear for all day; he would make an appointment with his wife and forget to keep it. He had no insight into or realization of these difficulties. He would wander all over New York and say nothing about it, nor consider it strange. He swayed more and more and tended to drag his left foot.

On Jan. 13, 1931, Dr. Scott reported: "The patient came in complaining of dizziness and 'wobbling of the feet' which began six months ago and was gradually getting worse; there were no headaches. The blood pressure was 120 systolic and 80 diastolic. Physical examination showed that the pupils reacted to light but slowly; the gait was unsteady; the knee jerks were hyperactive and equal; the Romberg sign was 3 plus; the Babinski sign was positive on the right and doubtful on the left."

On Jan. 23, 1931, the patient was seen by Dr. Scott and Dr. Starr; the latter thought that the condition was syphilitic and advised treatment with potassium iodide and mercurial inunctions. The patient was complaining of headaches. In the winter of 1930 and 1931, he had two attacks of acute follicular tonsillitis, which left him weak and with severe headaches. On March 19, 1931, Dr. Scott reported: "Unsteady gait was still troublesome, There were occasional attacks of headache. Lumbar puncture showed 33 cells, 100 per cent lymphocytes, and a faint trace of butyric acid. The Wassermann test of the spinal fluid was negative. The colloidal gold test was 1-1.5-2-2-1.5-1-0.5-0-0-0. The Wassermann test of the blood was negative. In spite of these findings, mixed treatment was prescribed."

In April, 1931, the patient was moved to the country. He had no violent headaches, but became worse mentally and physically. The gait was so bad that he had to give up work at the office and remain at home. There were no disturbances of the bladder or rectum.

On Jan. 14, 1932 he was seen by Dr. B. Sachs, who reported: "The pupillary reactions were normal. There was a marked senile arc. There was slight nystagmus on looking to the left. The knee jerks and ankle jerks were normal. The gait was cautious and uncertain. There was a slight Romberg sign with a little falling to the left. There was no trouble in repeating test phrases. Roentgen examination of the skull by Dr. Jaches gave negative results, except for thinning of the clinoid processes, probably due to long-standing pressure." Dr. Sachs thought that the diagnosis rested between an old cerebellar cyst and syphilis.

At subsequent examinations the following were noted: difficulty in concentrating on the simplest tasks; dulled mentality; slight ankle clonus on the right; distinct nystagmus of the right eye, and staggering.

In June, 1932, the patient had an acute attack of nausea and diarrhea; he was greatly prostrated and was confined to bed for three days. This attack was attributed to some clams that he had eaten. He recovered quickly. Because of diseased tonsils, tonsillectomy was performed, and he made an uneventful recovery. However, he was again prostrated and had to remain in bed most of the time, because he fell too often in attempting to walk.

On Aug. 14, 1932, one of us (L. H.) examined the patient at his home. He was out of bed but unable to get about without a cane. The eyeballs were prominent, and the pupils, normal. The disks were well outlined and showed a grayish pallor, but no papilledema. The patient complained of stiffness of the legs. After he walked a few steps the legs became so spastic that they were as if glued to the ground; he would remain fixed in that position and unable to move. The Romberg sign was marked in both directions.

The patient continued to complain of headaches and unsteadiness. Throughout this whole period, the blood chemistry, blood count and results of urinalysis were normal on repeated occasions.

On Aug. 23, 1932 the patient suddenly had a severe occipital headache; his face turned black, and he shrieked in agony. There was no loss of consciousness. For several days prior to this episode there had been incontinence of urine and feces. On Aug. 27, 1932, there was projectile vomiting. On Aug. 28, 1932, he complained of excruciating headaches and lapsed into periods of deep stupor. He had an attack of syncope and went into collapse, from which he recovered. On Aug. 29, 1932, he had a convulsion and died.

Neurologic Examination.—On Aug. 29, 1932, before the convulsion which caused his death, the patient was lying in bed, complaining of an excruciating suboccipital headache which he had had for about one week. There was no projectile vomiting, but nausea was present. He was well oriented in every respect. He was easily fatigued mentally and physically. Cooperation was good.

Head: There was no tenderness of the skull. The cranial segments and the peripheral connections were normal. Smell was not tested. The visual fields were grossly and roughly normal. The disks were well defined and of a grayish pallor, and the vessels of the fundi were not unusually congested. The eyeballs were prominent. The pupils were slightly dilated, equal and regular and reacted well to light and in accommodation. The external ocular movements were normal. There was no nystagmus, diplopia or corneal areflexia. Biting function and trigeminal sensation were normal. The facial motility was normal. Hearing was good. Vestibular function was not tested. The associated ocular movements were normal. There was no involvement of the soft palate, tongue or vocal cords. Taste was not tested. Deglutition was normal. The motility of the neck was normal.

Extremities: There was no paralysis or atrophy of any of the muscles. There were generalized weakness and flabbiness. Coordination was good. In the finger-to-nose and the heel-to-knee pointing tests there was some uncertainty, but no more than would be expected in a person who had been weak and sick for a long time; there was no frank dysmetria. There were no tremors.

Reflexes: All the deep reflexes were active. The right knee jerk and the right ankle jerk were more marked than the left. The abdominal reflexes were active and equal. There was a bilateral extensor response of the big toe.

Sensory Examination: Touch, pain and position and joint sense were normal. There were no meningeal signs.

Necropsy.—The brain was pale and showed a marked pressure cone consisting of the medulla and the tonsils of the cerebellum. The vessels at the base were not remarkable. The pia-arachnoid over the pons and medulla was somewhat thickened. The pons appeared to be flattened and somewhat widened. The medulla was obviously enlarged; it measured 3 cm. in the lateral diameter and about 2 cm. anteroposteriorly. A sagittal section was made through the entire brain and revealed a large cyst of the cerebellum in the middle line, extending into the right hemisphere for a distance of 2.5 cm. and into the left hemisphere for a little over 1 cm. There was a mural nodule of tumor tissue, about 1 cm. thick, in the wall of the cyst, occupying the position of the fourth ventricle. This nodule was firmly attached to the floor of the fourth ventricle and extended along it for a distance of 2.5 cm. (figs. 1 and 2).

In front of the nodule was another cystic cavity, which took the place of the aqueduct of Sylvius and measured about 1.5 cm. anteroposteriorly and 3 cm. in the opposite diameter. This cavity was connected with the third ventricle by a foramen measuring about 3 mm. in diameter. The quadrigeminal plate was flattened on the anterior part of the roof of the cavity. The superior portion of the roof was made up of pia-arachnoid, apparently intact, but thin and transparent. The posterior wall of the cavity was made up of the anterior medullary velum and the vermis of the cerebellum.

The posterior part of the medulla was hollowed out into a cystic cavity, but there was no demonstrable connection between this and the other two cavities. Each cystic cavity seemed, indeed, to be independent of the other two.

The third ventricle was greatly distended, as were the two lateral ventricles. The foramen of Monro was enlarged on both sides.

The mural nodule was placed exactly in the middle line, and many small cystic cavities could be seen in it. Microscopic examination of sections of this nodule showed it to be a typical fibrillary astrocytoma (figs. 3 and 4). Some of the smaller cavities in the nodule were lined by large glia cells, which may have secreted the material filling the cysts. Presumably it was one of these small cysts which became enlarged as secretion was poured into it and eventually distended the medulla into the large cyst already described.

The dentate nucleus was easily identified on the left side just outside the wall of the cyst. On the right, most of the dentate nucleus had been destroyed by the pressure of the cyst, and only a vestige remained.

The optic nerves were sectioned and stained for myelin, neuroglia, nerve fibers and connective tissue. They were both well preserved, except for slight loss of myelin about the periphery.

The wall of the largest cyst was studied microscopically and found to consist of felted neuroglia fibers and cells. There was no increase of connective tissue.

It is presumed that the cranial cavity was from time to time decompressed automatically through the thin roof of the cavity which took the place of the aqueduct of Sylvius, and thus operative intervention was not necessary.

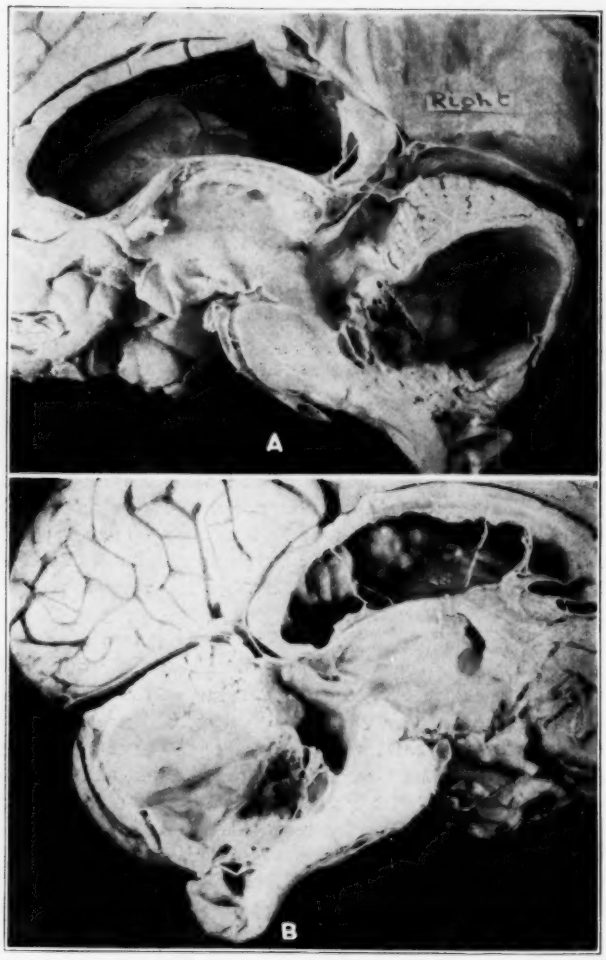

Fig. 1.—*A*, the right half of the brain, showing the cystic cavities in the cerebellum and medulla, with the aqueduct of Sylvius also ballooned out into a large cavity. The small cysts in the mural nodule of tumor tissue can be seen. The third ventricle and the lateral ventricle are greatly enlarged. *B*, the left half of the brain, with the three cystic cavities and the mural nodule cut in the middle line.

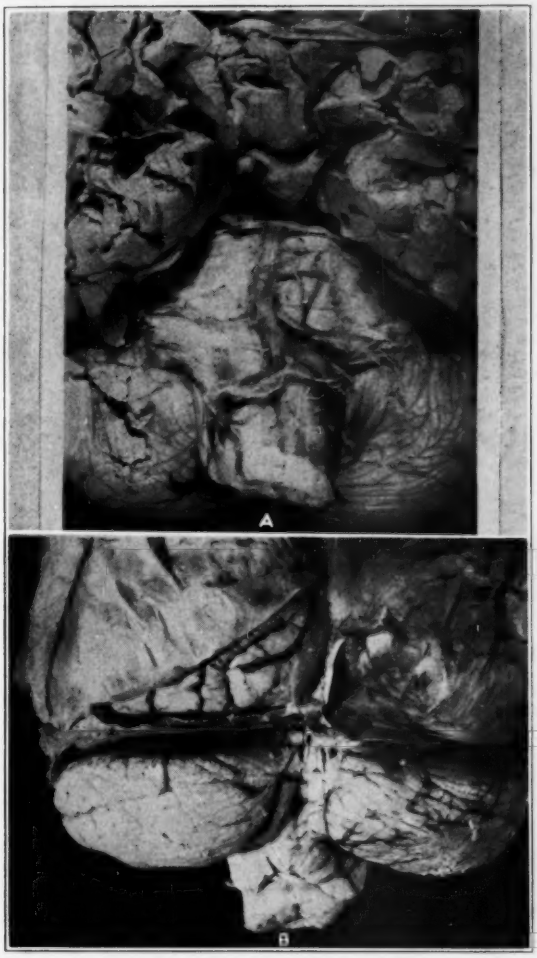

Fig. 2.—*A*, the flattened pons and the enlargement of the medulla. *B*, the pressure cone with the medulla and the tonsils of the cerebellum on either side of it occupying the position of the foramen magnum.

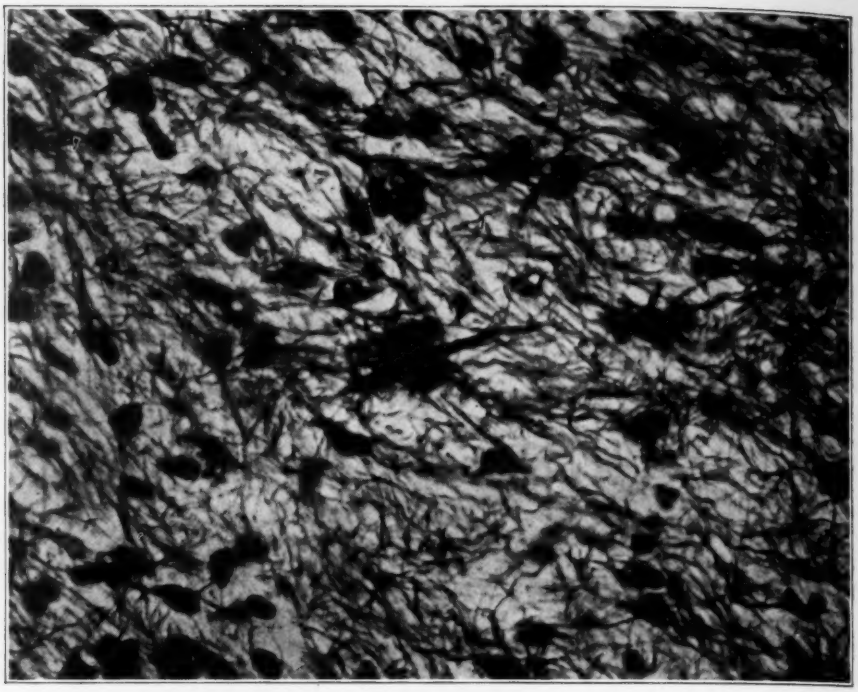

Fig. 3.—A section of the tumor nodule stained by Hortega's silver carbonate. Astrocytes and piloid neuroglia with abundant neuroglia fibrils can be seen.

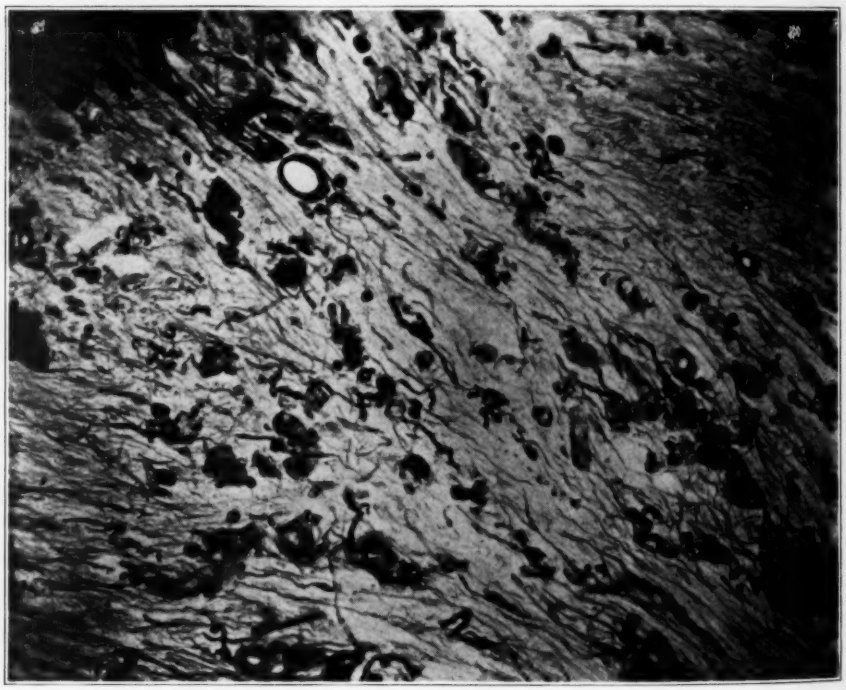

Fig. 4.—A section of the nodule stained with silver carbonate, showing neuroglia fibrils and nuclei and many blood vessels.

SUMMARY AND COMMENT

The striking clinical features in this case of astrocytoma of the cerebellum are. (1) the long duration (approximately forty-five years) without surgical intervention; (2) the acute onset; (3) the paucity of neurologic signs, despite their presence at the beginning (though the uncertainty of gait and difficulty in balancing persisted, the ability to attend to social and business functions was retained for a long time); (4) the long periods of relief from symptoms; (5) the episodes of collapse in the terminal stages, which probably were due to medullary compression.

The slow and interrupted symptomatic advance, with long intervals in which the patient was comparatively symptom-free, was typical of astrocytomas of the cerebellum, as described by Cushing in a recent critical review of seventy-six cases.[2]

The case is reported because the survival period of forty-five years is the longest on record. The fact that the patient was not operated on raises the question whether he would have done as well or better had surgical intervention been attempted even at the most opportune time. Certainly this sets a high mark for the surgeon to aim at in the records of survival periods.

DISCUSSION

DR. BERNARD SACHS, New York: It is unusual to have a case come under one's observation that has been carefully observed by others for many years. I do not know of any two neurologists of the last fifty years who examined patients more carefully than Dr. Seguin and Dr. Starr. Evidently Dr. Starr felt, as he had every reason to feel, that there was a cerebellar tumor but at that time operation in that region was entirely out of the question. I shall leave it to several of the surgeons who are present to decide whether, in view of the findings, they think the case would have been suitable for operation.

When I saw the patient in 1932, I felt that in all probability there was a cerebellar neoplasm, but in view of the fact that the case had lasted such a long time, there was some doubt that the first symptoms were the initial symptoms of the lesion that was forming. Moreover, the condition had lasted for such a long time that I supposed it must be a rather benign form of neoplasm and in all probability connected with some cystic formation, which was largely responsible for the give and take in the course of the symptoms. What disturbed Starr many years ago was a marked improvement on the giving of iodides. In cases of tumor marked fluctuation of symptoms following the administration of the iodides occurs, even if there is not the slightest reason to suppose that the neoplasm is syphilitic. I am glad to know that examination of the specimen shows no syphilitic involvement.

DR. CHARLES A. ELSBERG, New York: This interesting and well presented case gives additional evidence that tumors of the brain, especially the cystic varieties, and more especially cystic astrocytomas of the fibrillary type, last for a great many years and may exist for many years before they give symptoms. Every one who sees many tumors of the brain has had the experience that I have had during the past year, of observing a patient who had convulsive seizures since early childhood, who finally presented signs referable to an increase of intracranial pressure, and who was found to have a large cystic astrocytoma near

2. Cushing, Harvey: Experiences with the Cerebellar Astrocytomas. A Critical Review of Seventy-Six Cases, Surg., Gynec. & Obst. **52**:129, 1931.

the motor area. The question raised by Dr. Sachs is one that cannot be passed by without some remarks, namely: What was the condition years ago? Did the patient at that time have a cystic tumor or were there some other changes which produced an increase of intracranial pressure and which in the course of years resulted in the growth which finally caused death? Of course, on that would depend the answer to the other question asked by Dr. Sachs: Could something have been done for this patient surgically one or two years ago? If he had a cystic astrocytoma which at that time did not involve the structures that were finally involved, of course he should have been subjected to surgical intervention, and he might, if he had survived the operation, have been alive today. The question cannot be answered with certainty because one does not know the exact condition that existed a number of years ago.

SPECIAL ARTICLES

PREPARATION FOR PSYCHIATRY

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Whenever a physician assumes the special title of psychiatrist, indicating a special preparedness to deal with the person and personality functions, it becomes mandatory that he should have a reasonable training. A title carries expectations and a responsibility. What should this include?

Medical practice and medical education have been greatly influenced by the developments in what one understands by "pathology and therapy." "Pathology" has been, and to this day is, limited largely to the sphere of the owner of the corpse and of the microscope. Even "clinical pathology" today makes one think of the laboratory and the roentgen-ray room. Unfortunately and unjustly, the data accessible during life are called or thought of as "symptoms" instead of data of pathology, much to the confusion of thought—as if diagnosis and therapy were not pathology at work! One has to accept both functional and structural data of pathology, more and more on an experimental rather than on a statically descriptive basis, including also the disturbance of function by collisions of functions. Therapy, too, especially in the field of "borderline cases," has gone through many phases. Predilection used to range, and indeed still ranges, from the "fat and blood theory" and a rest cure through elaborate electric displays to hydrotherapy and massage, travel and possibly some hypnosis and therapeutic conversation. Until quite recently, there was a popular and professional cleavage into what could be handled outside of specially licensed institutions and what required commitment, i. e., treatment in a licensed institution. There are, however, two things that disturbed this apparent simplicity: the arrival of the problem of the delinquent child and the arrival of voluntary commitment for psychotic persons, in both of which the psychiatrist's help was sought under novel conditions demanding more individual attention. Moreover, especially since the end of the eighties, there had developed a special field of psychopathology and psychotherapy, in practice and theory strangely separate from psychiatry and clinging rather to neurology because of economic and traditional exigencies of popular practice: at first largely hypnosis, then persuasion and more and more the freudian and allied methods. From a theoretical point of view, too, there had moreover come a rise of psychology from

a dualistic introspective seclusion to a position in the world of action, particularly through the popularization of the intelligence and vocational tests and the exploitation of abnormal psychology in the ordinary non-medical college course.

NATURE AND SCOPE OF MODERN PSYCHIATRY

Actually, today, psychiatry defines its domain as the study and treatment of all abnormal conditions in which are involved man's behavior and mentation, or, in one word, ergasia (in root and meaning a word identical with "working"), that is, mentally integrated behavior or functioning. The term ergasia is used because "behavior" yields no plural and because the adjective "behavioristic" is apt to characterize not the type of function but the theory, such as that of Watson or McDougall or some other theory. Ergasia and its derivatives are intended to put emphasis on critical common sense and objectivity. Without quarreling with that traditional psychology which chooses to start with elements of sensation and affect and conation—to my mind, not elements but maximal differentiations—the practical worker gives even the subjective data their status of objective reality or actuality. There has consequently developed more and more clearly an objective as well as a subjective psychobiology, which observes attitudes, actions and mentation for their meaning and importance in the larger and obvious life functions of the human being and which refuses to split off a "mind" with an absolute and detached existence, and looks on attitudes, actions and mentation as specific types of organismal behavior, as functions among other functions, as ergasias or performances in a flow of representative function making up the biographic record of the person. In spite of being hereby on the ground of sound critical common-sense usage, it will not do to assume that the average student will handle this type of fact without disciplined training. The physician is often outflanked by social workers with present-day training, and is shown to be remarkably helpless and loose, officially intimidated and prevented from making a frank use of his common sense by the charge of its being unscientific and unworthy to be considered in the formulations of real pathology. What is wanted is a training in dealing with functions as "experiments of nature," i. e., a genetic-dynamic conception of reality and actuality.

A course in psychobiology organizes the significant "experiments of nature" presented by the normal person or group and studies them for their working together. It regards the mentally integrated character of ergasia not as a mere "special mental aspect" nor as a mere epiphenomenon; it does not split off a parallelistic largely introspective datum but deals with the mentally, or more or less consciously, integrated function and performance itself in a specific person's life (or I

had better say living, so as to avoid the naive tendency to suspect any one mentioning "life" of either a kind of mystical vitalism or just a kind of "mechanism"). What is actually implied is that it recognizes the organismal physical nature of the person and the nondetachability of the functioning, which forms an integrate of a specific type and not an extraneous superaddition. Modern critical common sense thus comes closer to the facts and their management than most of the traditional types of formal psychology. Psychobiology trains this common sense and assumes that all can agree on the generally accessible behavior including mentation as objective and specific data and relations. Its subject matter is the functioning of a very physical organismal entity or person, palpably visible in any movie, observed for the personality function or personality formation, the ergasias (behavior or conduct) of the real and undivided "he" or "she," whereas physiology studies the function of detachable parts or organs. Psychobiology deals with the biographically organized total functions or personality functions, while physiology focuses more specifically on the methods of physics and chemistry applied to special organs, relatively free from psychobiologic considerations and relations. These sets of facts interpenetrate as specific mentally integrated (psychobiologic) or nonmentally integrated (physiologic) data of concern and are not merely "different aspects." The day should be passing when any person should consider himself educated without a reasonable orientation among all the sciences entering the field of biology: anatomy and physiology including structure and function of the parts, psychobiology treating of the mentally, or more or less consciously, integrated function of the person or individual, and sociology presenting psychobiologic functions of the groups. Neurology may disregard, but certainly cannot do justice to, the psychobiologic combinations and their share in the life of persons; but psychobiology does not ignore the neurologic and general physiologic and physicochemical components of the "experiment of nature" with which it deals. The neurologist can as little as any other physician afford to ignore the psychobiologic or "behavior and conduct mentation" data of the person on whom he works. Yet, making the brain and nervous system his central issue, he treats the personality functions as a secondary concern; similarly, the psychobiologist dealing with the individual as his unit treats neurology and general and special physiology and the physicochemical data as incidental or inherent data, as part of the internal and external situation or state of affairs. The "psychopathologist" may then focus on the specific factual data of mentally integrated attitudes, reactions and actions; the "psychiatrist," however, must also be able to assume general medical responsibility.

To repeat, the psychiatrist must be primarily a physician, but one specifically trained to occupy himself not merely with the function of

parts but with the personality function, the characteristic of which is that it is "a story in the making," a part of a biographic development (in contrast to the more mechanized function of parts), operating with the help of mentation or sign function or symbolization, overt or implicit, and with its characteristic selective and constructive plasticity.

UNDERGRADUATE TRAINING

The training of the psychiatrist must develop his available critical common sense concerning the personality functions in addition to the part functions, and must include a thorough general medical training. Instead of making the student feel as though he merely had to add some psychoanalysis or other special training to his equipment, one must insist on his developing consideration for the use of the heart as such but also in emotion, the ear and the larynx as such but also in verbalization, i. e., the working of the parts as such but also in personality functions, if possible from the beginning of his anatomic, physiologic and therapeutic training. At the Johns Hopkins University Medical School, psychobiology is a required subject in the first year as a necessary supplement of training in anatomy and physiology. It is carried on as a personality study, with discussions of the material and its function as the study proceeds. The emphasis of the training is laid on the motivation and setting as well as on the intrinsic working of the behavior patterns and developments of normal life. In the second year one turns from the normal to the less normal, and to the study of the methods of examination and the formulation of the data into reaction sets. At the same time I give an elective course in neurology organized so that it falls in line with the conceptions of the course in psychobiology and gives the latter a solid foundation, without becoming either neurologic tautologizing of psychobiology or unjustified psychologizing of neurologic data. The same interdependence and yet distinctiveness might be expected of the working together of psychobiology with physiology throughout pathology, internal medicine and surgery. None of these fields can be treated without some concern for the other components of the picture and setting. From the very beginning of the contact with patients, the student is made to realize that there are psychobiologic questions (the person's attitude, behavior and range of mentation and performance in conduct) which in some patients and some disorders become the leading issue and concern.

PRINCIPLES UNDERLYING CURRICULUM, UNDERGRADUATE AND GRADUATE

As a teacher of psychobiology I regret the present-day trend of American medical schools to partition the training unduly and to focus too one-sidedly on laboratory work. Every possible emphasis should be

laid on the work also with the living person as the way to maintain a balanced program. The English training and the French training have perhaps a better perspective. I also deplore the tendency to let special departments appropriate students before they have acquired the necessary breadth of base on which to stand. Particularly in psychobiology, it becomes difficult to make up for neglect when attention to its topics is deferred to a later period. It surely cannot be any longer the ambition of natural science to make preoccupation with "the total functions or mentally integrated functions" unnecessary or to refer it to others; on the contrary, science should frankly accept responsibility for what psychobiologic data the living being presents. An interest in the person only where hypnosis, suggestion, intelligence tests or psychopathology begins is poor science and poor practice in teaching and understanding. For this same reason, I am definitely of the opinion that the student cannot afford to detach himself from a certain amount of clinical work or contact with patients at any time throughout his training, and this should as soon as possible take the form of specific responsible tasks and performances. In other words, medical training (and all human training) had best be given in the form of an apprenticeship, but with ample time for digestion of the practical experience and with systematic work in organized courses whenever this is possible.

The basic undergraduate and special graduate training should come from persons who have practical contact with the various phases of life: the prenatal and the natal period; the infancy stage; the nursery and preschool period; the primary school phase; the adolescent and the young and the advanced adult period; the mature years; the involutional and the senile stages. And with this should go a familiarity with the situations arising in each of the phases. There is a burning need of concreteness and at the same time of concentration under the guidance of sound practice, with practical work balanced by the principle of a kind of natural selection, and this means that the practical work has to be well enough organized to give the student his contact and experience first close to the school of life and then, when he begins with pathology, close to actual clinical material in the admission wards, the intermediate wards and the division for "neurotic" (i. e., minor psychotic) patients and for convalescents.

Special attention should be given to securing concise and effective presentation of the data on ward rounds, in staff conferences and in records of interviews with the nurses, relatives, the home physician and the patient. Moreover, the plan of training has to include the outpatient department with its reports of the examination of patients furnished to the various agencies, treatment of ambulant patients on an appointment basis, consultation work for the other departments of the hospital and service in pediatrics and in the departments of internal medicine, sur-

gery, urology and syphilis. Moreover, a period of work in a state institution providing both clinical and autopsy and administrative work is obligatory, and also work with schools, with the juvenile court and with medicolegal issues. A two-year or, if possible, a three-year program should be considered the minimum for a well rounded basic training for one entitled to the name of psychiatrist. Systematic alternating shifts of emphasis on ward and special work should give time and opportunity to digest the experience. The various psychopathologic and psychotherapeutic procedures and the literature and methods of the various schools must be assimilated.

As psychiatry is much broader than psychoanalysis, the latter is to be regarded as an incident in the broader training, to be limited to specially talented physicians and well chosen patients; it is not to figure as the all-pervading principle of actual psychiatric practice. A question that provokes the greatest diversity of opinion relates indeed to the scope granted or required for psychoanalysis in a scheme of training in psychiatry. Unless a physician has a special urge, need or talent in this direction, it is a question whether a routine requirement of psychoanalysis does not become a distraction and disruption of the habitual procedure and orientation for both the patient and the physician. This should not, however, imply a disregard of the broadening of the rich material of content and motivation that the psychoanalytic workers have contributed. Indiscriminate mixing of principles or a belief in exclusive salvation is, however, often detrimental to both practice and patient. In the main, in spite of the value of personal experience, I am a bit suspicious of those who have been psychoanalytically trained chiefly because they needed to be psychoanalyzed on account of their own maladjustment or who had to be aroused by the lure of the revelations. To be able to be a sound psychoanalyst requires an exceptional combination of elasticity and critique and medical training. I should advise a good training in the most rigidly disciplined psychiatry and psychobiology before the intensive training in any form of psychoanalysis if this is still possible and compatible with actual practice and conditions of work. For the rank and file, training in distributive analysis of the determining factors and synthesis of the physician's and the patient's positive and negative assets is the best that can be offered and used.

In addition to the ideal complete program, there naturally must be opportunities for shorter courses, as well as visits to differently organized centers, with the obligation to report the special observations.

Teaching centers are most advantageous for training, but periods of work in centers for intensive practical work are also essential. Whenever possible, the psychiatrist in training should also have experience in teaching, so as to make himself responsible for well organized formulations.

Intrinsic understanding of the patient's state and situation, reconstruction of nature's experiment and constructive handling of the "pathology and therapy" in specific cases and groups of cases must be cultivated above all things.

As to laboratory technics, psychologic or otherwise, I believe that in the main no "tests" should figure as urgent and convincingly valid until they tempt the ward physician to try to master them himself. While some work may be left to technicians, it should never get far beyond what the physician should be able to do or to know thoroughly in its principles and to sense the value of. Otherwise one drifts into the present-day superabundance of work that "can always be done" but is often done as a mere show of thoroughness without regard for the patient or for economy of time or money.

The training must have as its goal a preparedness to meet the rank and file of practical cases and the emergencies of psychiatric experience. And to reach this goal, graduate study in psychiatry should always take the form of assistantship, and the assistantship should be of a type that allows time and opportunity for the digestion and supplementing of the practical work with a reasonably systematic course in which a more detailed study of personality and laboratory work in neurology and in psychobiology and in all the fields drawn on in behalf of the patient find their place and time for assimilation.

COMMON SENSE

Whatever one may wish to learn in psychology or psychobiology, the first step must be to organize what common-sense knowledge one possesses and whatever methods the student brings to his patient. I heartily disagree with those who so distrust even the most critical common sense that they ask for new oversystematized concepts and terms with a clean sweep of all the old. With regard to terminology, I consider it easy to show that the precipitate of human experience shaken down in the natural development of language is infinitely closer to reality than the "high-brow" use of special terms would often indicate. There is no objection to any real enrichment of language and modes of presentation, but the first step is what might be called an interest in the facts close to reality and life, and the use of the best available terms, with plenty of exposure of both the language and the facts to the critical sense demanded not only in Missouri, as the phrase goes, but as a general commodity. The days of verbal magic are unfortunately not over, but it does not overawe the average person today. Plain facts and plain words are needed first, to be supplemented by what corrections prove necessary in the light of constructive and critical experience.

No student who has not a sense for meanings (be it of looks, of utterances and posture, of behavior, of characters or of means of help-

fulness) should enter psychiatry. And by "sense" I mean a natural and practical critically minded and not merely verbal response. Whoever has to be stirred first by the extraordinary or by his own psychobiologic discomforts and preoccupation is hardly the best material for psychiatry. The psychiatrist as a mere "diagnostician" or as a mere sympathetic bystander comes closer to being a racketeer than a physician. There is the greatest need for imagination and its critical, and especially its constructive use, but it must rest on a solid basis of well disciplined common sense.

RELATION TO OTHER DISCIPLINES

It is not half so difficult to say what is the best course of training in psychiatry as it is to state what can be done to assure a sound orientation toward the subsidiary disciplines likely to affect the aspirant, to use Dr. Walshe's term [1] (whose appeal for bedside pathology—if he permits this term—supports my prejudice in favor of what I should like to see understood as real pathology and as apprenticeship). Sound orientation implies a capacity to include the psychobiologic facts and methods and problems that one must observe and work with. The lingering nineteenth century philosophy of science still fails to naturalize man or to humanize what is to be applied to man. As stated, I should begin with a demand for sound common sense and sound general medical education, with an intimation that medical education does not always include common sense and is apt to be psychobiology-shy. Dr. Walshe's advice to spend, between the preclinical and the clinical preparation, an extra year in a laboratory has my approval if it includes neighborly relations to psychobiology. Otherwise, it may remove the student even further than usual from devotion to the critical common sense that he needs in psychiatry. This holds also for work in medicine, surgery and pediatrics, and by no means least in neurology, gynecology and urology and whatever other emphasis in the total picture makes up the general medical prerequisites for any specialist's training.

As soon as the rest of medical training recognizes its obligation to pay reasonable attention to the person and to personality function as part of all physician-patient relationship, it will be possible to consider an internship in one of the general medical branches an important part of the foundation for psychiatric graduate training. When but inadequate emphasis is given to the human problems, special postgraduate training in internal medicine and other specialties might as well be inserted later when the psychiatric aspirant has acquired his own sense of relations and proportion.

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1. Walshe, F. M. R.: Training of the Neurologist, Arch. Neurol. & Psychiat. **29**:368 (Feb.) 1933.

Anatomy without ample study of the living, physiology without ample inclusion of general biology and respect for the psychobiologic total functions and internal medicine or neurology taught by persons not also at least psychiatrically intelligent would not be altogether sound or safe or desirable unless there was serious contact with the psychiatric staff.

Above all, one needs in psychiatric training a sound blending of the study of things as they are found in patients, and not only a study of what one finds in the contents of the test tube and in special experimental preparations. Nobody can furnish or find that sound blending in an atmosphere not friendly to the present-day views of man and a natural science including man, "body and soul"—not for mere possession as one's patient or one's autopsy material, but for work. One can avoid the "seven and twenty jarring sects" of the new psychology referred to by Dr. Walshe by training the student at least to use the sense he is born with and to learn to improve it by the use of his own experience and all the guidance that fits into it.

How much internal medicine should be studied?

From the angle of observation and study it is especially important to know the "normal" and also the unavoidable variations of functions which the average physician is taught to disregard so as to avoid being misled into false diagnoses. The psychiatrically intelligent internist does not disregard but learns and teaches how and where to assign "functional" symptoms and "nervous" signs and complaints of the various organs and functions. Whoever specializes in psychiatry must know the range of variations of heart dulness, heart sounds and heart rhythm, indeed all the things which the beginner is taught not to mistake for evidence of lesions (or as medical jargon will have it, evidence of "pathology"). The same holds for the gastro-intestinal tract, the skin, metabolism, the endocrine glands and other organs. Present-day pathology is not only anatomy and histology but fully as much a variant of physiology, and is greatly interested in findings that are often tossed aside unused by those devoid of a genetic-dynamic orientation.

This same point holds for neurology. Many a good "organic" neurologist is a poor trainer for the neurology needed by the psychiatrist or average physician. It is often the "nonsignificant" and "noncontributory" variants that count and with which one must be familiar, not for the purpose of discarding them but to give them their due. With all my love for the structural facts in neurology, I greatly deplore the paucity of help and training offered in the organization of functional data. My introduction to anatomy of the brain [2] is one of broad func-

2. Meyer, A., and Hausman, L.: A Reconstruction Course in the Functional Anatomy of the Nervous System, Arch. Neurol. & Psychiat. **7**:287 (March) 1922; The Forebrain, ibid. **19**:573 (April) 1928.

tional lines. Function demands a training that should become available simultaneously with the anatomic and physiologic discussions and clinical study. Moreover, the closer one comes to the sympathetic and parasympathetic balance and the postural reflexes and to the problems of aphasia and apraxia, the closer one gets to common interests and common needs of the anatomist, physiologist, neuropathologist and psychopathologist.

POSTMORTEM STUDIES

Even pathologic anatomy—unavoidably sadly managed by the general pathologist not clinically trained—is safe only in the hands of one trained in a psychiatrically intelligent neurology.

Deplorably little is being done along the lines of complete investigation of autopsy material. Good and convincing experiments of nature and accident are rare. They should not be lost under the impression that all the work has already been done. There is too much teaching not constantly controlled by study of actual material. Practically no material of vital importance has been added to the study of secondary degenerations coming out of experience in the World War. The International Brain Commission has gone out of existence, and systematic studies requiring special laboratories are scarce. This is bound to revenge itself on the quality of teaching and preparation of the new generation.

GENERAL CONSIDERATIONS

The first condition for sound psychiatry consists in the gathering and recording and coordinating of the data with which one works and by which one is guided from day to day and through the lifetime of patients.

It is fairly well agreed today that the facts must be accepted in the form in which they are most distinctive and also most controllable, either by corroboration in reobservation or, whenever possible, by test, i. e., by performances obtainable at any time. The latter desideratum must be recognized as only partly attainable. Man is an entity that does not respond in an invariable manner. Even in the organically definable disorders, only a limited number of performances are constant and obtainable in a uniform manner at all times. Almost all reactions are apt to vary somewhat from day to day, and a large number are bound to be relatively unpredictable, but reasonably true to type if one makes allowance for the obligatory relation to situation and the personality. The most characteristic and personally distinctive data must be gathered and accepted as personal and considered in the light of a history. To discard the historical specificity of human life and development in favor of the nonhistorical physiology would be fatal to accuracy. The data concerning a person are fractions, with the

concrete performance as numerator and the broader life data as denominator, and with even the denominator necessarily changing with every progression of additional life experience. Statistical work on persons that does not heed these concrete numerators and denominators has but a limited sphere of validity. Statistics do not give more than probabilities. Each specific case and instance calls for a summary consideration of the specific problems, assets and issues, and the type of combination. Consideration of these points then leads to the genetic-dynamic conceptions if one aims at dependability of the inferences, and to a frank espousal of reaction sets which must not be taken as finalistic diagnoses without a checking up covering the various sets of possible relations—exogenic, organogenic, neurogenic, constitutional and psychogenic. Only cases with sufficiently similar and comparable fractions should be compared and used as a basis for generalizations. One gradually works out standard types as approximations to something like working units, within which one may more profitably undertake more highly detailed and specific inquiries and correlations. Under no circumstances can one forego the consideration of both individual and generic factors.

All this requires a capacity to master one's actual range of data in a dependable manner. Moreover, for the organization of one's experience it is essential that one should have a body of sufficiently long controlled cases. Indeed one should have enough cases that have been seen through to the end and to autopsy, and, I trust, some time, studies of a number of generations.

RESEARCH

Within this setting, and only within it, is there a place for research in the realm of part disorders or part functions in the physiologic and other special realms.

The desire to introduce chemical and internistic work by persons not trained in the psychiatric patterns and settings and not in touch with the daily variations and the long-term perspective leads oftener than not to disappointments. Yet hope in these directions must be fostered because of the far greater dependability and accessibility of the quantitative and unconditioned data.

My experience leads me to the following conclusions: Whoever wants to do research in psychiatry must have a basic general training in psychiatric observation. Without that the special worker will lose himself in grinding the organ of extraneous methods and problems, usually with scant bearing on known psychiatric issues. Far more has been achieved in the gains from detailed long-term study and efforts in real psychiatry than with the methods indiscriminately introduced from general medicine or other special domains. Even the modern

treatment for dementia paralytica came from a psychiatrist and not from a specialist in syphilis.

No one can say *a priori* along what lines genuine advances are to be made. Nevertheless, when one reviews the attainments of the last sixty years, one finds that progress has been partly in the direction of a more determined and intelligent use of the personal assets along individual lines and also along the lines of socialization and personal adjustment. There is need of a singling out of conditions within which special helps can be determined and introduced; the procedures are largely individualized and are by no means as strongly "mechanized" as certain psychotherapeutic formulas would lead one to expect.

The future of psychiatric research will depend partly on chance, but largely on the creation of sound conditions for practical psychiatric work satisfying and attracting good workers with enough interest in training for specialized work.

SUPPORT FOR FOLLOW-UP AND RESEARCH WORK

Research in neurology and psychiatry serves cultural rather than immediately practical usefulness. Most of the special work of inquiry goes beyond what the individual patient should be forced to pay for. Nevertheless, to be a good neurologist and psychiatrist one cannot remain a mere routinist. Considering the amount of opportunity to learn from experience in neurosurgery, the habit of securing and maintaining follow-up work that cannot properly be charged to the patient deserves more extensive support than it has today, as part of neurophysiologic training and research. All this depends on sounder methods of working together, sharing opportunities and conveying to the agency able to support research a sense of where support is needed and the responsibilities for progress lie. What can be more important than more knowledge of the integrative functions of man and human life? Can one go on leaving it to the philosopher and theologian on the one hand and to the physicist and chemist on the other, and missing the experiments of nature with the actual human being? How can one give opportunities to see the actual working of psychiatry unless one can overcome the systematic ignorance and inattention with regard to the nature and working of human nature?

PUBLICATION

It is quite probable that for some time to come a reasonable amount of continence in publication is more of a virtue than a cause for reproach. Particularly in the direction of "mental hygiene," publicity and promises of therapeutic boons, a more conscientious adherence to what can be proved and used is greatly to be desired. It is all the more necessary to secure adequate support for publication which may require more

space than the average medical article or monograph, on account of the need of specification of the settings and the great differentiation of the psychobiologic data and the checks introduced from contributing fields—so valuable, provided that they can be said to be contributive.

TEMPERAMENTS NEEDED IN PSYCHIATRY

There is room for many different temperaments. There is a demand for administrators, who must know the needs of both patients and physicians and also the general public and who must, moreover, know fiscal conditions. Intimate therapeutic work with individual patients is one thing, the talent for socializing hospital treatment often another. There are socially interested psychiatrists working in outpatient departments, schools, factories and courts, all in need of sound knowledge of the generally accessible facts in the cases and also of the needs of the families, friends and public and trends at large. There is need of safe, constructively minded relations to the community. There are coordinators and persons who take to details. In the end all have to acquire a capacity to review and grasp the broader relations as well as the more and more specialized hobbies, and to build up a genuine consensus with freedom and solidarity.

SPECIALIST AND LAY WORKERS

Some difficulty arises from the need of defining the spheres of work of specialists and also of lay workers. To the nurses belongs the cultivation of what makes for the best twenty-four hours of the day, supplementing rather than imitating the physician's work—a sphere of great usefulness, if they take seriously their unique opportunities without the burden of the detail confided to and demanded of the physician. Taking histories and seeing relatives and friends should not be relegated to nurses. It should remain an important opportunity of the physician. Psychologists must find it difficult to outline their sphere if they reach into the practical working with patients. McDougall justly advises that all those who wish to work with mental disorders should supplement their psychologic training by an adequate medical training. The analyst usually takes over the patient altogether; so does the theologic healer. There are frequent complaints that psychiatrists fail to understand the cultural aspects and the sociologic aspects of the lives of their patients. Much damage to medical usefulness comes from this gap—something to be remembered in cultivating the premedical and extraprofessional interests.

DIPLOMA

There are efforts under way to clarify the requirements for recognition as psychiatrist. All physicians should be familiar with the funda-

mentals of psychiatry. The specialist must be able and prepared to show and state what he expects to be the chief problems and opportunities for work and treatment.

A standardized examination of candidates for a diploma is difficult to conduct except in connection with actual work and with a determined review of the pertinent disciplines and teachings and surveys of current literature and the handling of new material.

In consideration of the importance of familiarity with more than the literature in English, attention must be given to early training and practice in German and French at least. The use of the linguistic facilities and the available range of literature and the manner of its use and organization should appear in the summing up of the actual case material and the reports of the labortory work. The actual record of training and practical and scientifically organized work cannot profitably be fixed arbitrarily, but should figure greatly in the evaluation. It is expected that the development of organized graduate courses and specifications of the standards of the several subspecialties in neuropsychiatry will give increasing definition and concreteness to the scope of requirement for both the candidates and the examiners. One must demand not only that the diploma should protect the public, but that it should be a guide and stimulator to progress in the study and care of patients and in the spreading of sound practice and attitudes in the medical profession and in the public and in the cultural life.

CAREER

The outlook for a career, as in any other field, depends on the personal equation and capacity for service. A growing range of institutional and personal work is open with promise of a very worthwhile position professionally and socially and as a teacher. Perhaps, when more persons become educated not in natural sciences only or in humanities only but especially in the study of man as he actually grows and functions and becomes an asset or a handicap to self and to living humanity, one may look for the support of psychiatry and its contributive sciences as a task of advancing culture even if the benefit to the individual sufferer cannot be as individually gratifying as one would wish. Man grows but one brain in a lifetime and is thereby likely to be limited in his personality development. One cannot let progress in psychiatry depend merely on its earnings from its cases in the same sense as progress in surgery and many other branches of medicine does. On the other hand, cultural advances based on scientific rather than on emotional revelation will be needed to meet the basic conditions for advancement of the race, and, having to depend largely on "experiments of nature," one can expect worthwhile experience from the psychiatrist

who does not have to cater to fashions and to emotions as much as has been the case in the little more than a hundred years of the existence of psychiatry as a planned pursuit.

SUMMARY

Psychiatric training calls for a plan of apprenticeship with enough systematized presentation and amplification of the concrete work with individual persons. It rests on experience with personality study of normal persons and of persons with special complaints and problems, the reduction of the history and examinations to terms of an experiment of nature, with emphasis on the balance of the plastic modifiable and the nonmodifiable components of the person as a unit, in contrast to either physiology or sociology.

It is an intrinsic part of all medical work.

Specialistic training includes apprenticeship in a teaching center with an adequate range of practical experience in ward, laboratory and field work, liaison activity and theoretical organization of the material.

It assumes a sound conception of the relations of pathology and therapy in a setting of biology recognizing psychobiology as the division of total function or personality function.

CONSTITUTION AND BY-LAWS OF THE AMERICAN NEUROLOGICAL ASSOCIATION

HENRY ALSOP RILEY, M.D.
Secretary
NEW YORK

The publication of the Constitution and By-laws is deemed advisable in order to call attention to the new requirements for admission to membership in the American Neurological Association. It is hoped that similar requirements will be universally adopted as a criterion for the necessary training of neurologists.

CONSTITUTION

ARTICLE I

Object and Name

The Association shall have for its object the advancement of neurological science, and it shall be known as the American Neurological Association.

ARTICLE II

Members

The membership of the American Neurological Association shall consist of Honorary, Senior, Active and Associate Members. The professional and scientific qualifications which establish the eligibility of any candidate for the various types of membership are presented in detail in Article IV of the By-Laws.

Honorary members are those who by reason of professional and scientific qualifications are deemed worthy of such election to the Association.

Senior members are those who have been active members of the Association for twenty-five years and have reached the age of 65 years.

Active members are those who may be elected to such membership by the vote of the Association. The number of active members shall be limited to 175.

Associate members are those who may be elected to this type of membership by reason of special and particular interests.

The Council shall have power of decision in the consideration of each candidate's eligibility and its judgment upon such eligibility shall be final.

Senior and active members alone are qualified to vote and hold office.

ARTICLE III

Forfeiture of Membership

Membership shall be forfeited by failure to pay the annual dues for three years or to attend three successive meetings of the Association without an excuse deemed sufficient by a majority of the Executive Session. When an excuse has been

accepted, attendance of the member or an excuse acceptable to the Executive Session shall be required the following year. The Secretary shall, three months before the annual meeting, notify members liable to forfeit membership on account of nonpayment of dues or nonattendance, but failure of the member to receive such notification shall not relieve the member of responsibility. The presentation of an original paper at an annual meeting shall be deemed equivalent to attendance. Membership may also be forfeited for reasons deemed sufficient by the Association, provided such forfeiture be recommended by the Council and approved by an affirmative vote of three fourths of the members present at an annual meeting.

ARTICLE IV

Officers

The officers of the Association shall be a President, two Vice-Presidents, a Secretary who shall also be Treasurer, and an Assistant Secretary, all of whom shall be ex-officio members of the Council, all to be elected annually. There shall also be five Councillors, one to be elected each year, for a period of five years. The Editor of the Transactions shall also be a member of the Council, ex-officio, without a vote. At the annual meeting following the Congress of American Physicians and Surgeons, the President shall appoint a member and alternate for the Executive Committee of the following Congress, and a member and alternate for the Committee of Arrangements of the following Congress. At the first executive session of each annual meeting the President shall appoint a committee of three to report, on the following day, nominations for officers for the ensuing year.

ARTICLE V

Editor of Transactions

An Editor of the Transactions shall be elected at an executive session of each annual meeting. The Editor shall secure the papers read, and a suitable report of the discussions thereon, and shall prepare and edit the annual volume of the Transactions.

ARTICLE VI

Duties of Officers

The duties of the President, Vice-Presidents, Secretary and Treasurer and Assistant Secretary, shall be those usually assigned to such officers. The Council shall meet as often as the business of the Association shall require, and four members of the Council shall constitute a quorum. The Secretary shall also act as Secretary of the Council, and shall, on the first day of each annual meeting, read a report of the transactions of the meetings of the Council and of the financial status of the Association. The Council shall not have the power to make the Association liable for more than $100 in any one year, unless authorized to do so by vote of the Association. The Council shall make arrangements for the annual meetings and rules governing the presentation of papers.

The President, Secretary and the Editor of the Transactions shall constitute a program committee which shall be responsible for the preparation of the program for each annual meeting.

The Program Committee shall arrange in advance a symposium on a given subject to be presented at one of the scientific sessions of each annual meeting. The

Council may, for sufficient reason, direct the omission of the symposium from the program of an annual meeting.

The representative on the Executive Committee of the Congress of American Physicians and Surgeons shall have full power to represent the Association on all ordinary questions, but he shall not assent to the admission of any society to the Congress without an affirmative vote of the Association at an annual meeting.

ARTICLE VII

Meetings

The Association shall meet annually, at a time and place designated by the Council. The President shall call the meeting to order. In his absence, one of the Vice-Presidents shall preside. Original communications shall follow. The reader of a paper shall not exceed twenty minutes in the presentation of his paper, and no one shall speak longer than five minutes in the discussion of a paper. Members must send the titles and abstracts of their papers to the Secretary at least six weeks before the annual meeting, and the Program Committee shall decide what papers shall be read and shall send to each member a program and abstracts of the papers to be read at least two weeks before the annual meeting.

ARTICLE VIII

Quorum

Twelve active members shall constitute a quorum for the transaction of ordinary business, but for the election of new members, twenty shall be required; and for changes in the Constitution, twenty-five shall be required for a quorum.

ARTICLE IX

Dues

Annual dues shall be determined by the Council and an entrance fee will be required from newly elected active members, but honorary and associate members shall be exempt from all dues.

ARTICLE X

Amendments

Amendments to this Constitution must be made in writing at an annual meeting and must be signed by five members. They shall be voted on at the next annual meeting, the announcement of which shall contain the proposed amendment. Such an amendment shall require an affirmative vote of two thirds of the members present to be adopted.

BY-LAWS

I. *Executive Transactions.*—All business not of a scientific nature shall be transacted in executive session. There shall be three executive sessions during the annual meeting, one at the close of each morning scientific session. Special executive sessions may be called by action of the Council.

II. *Order of Business, Scientific and Executive.*—The order of business at the annual scientific sessions shall be (*a*) The Presidential Address; (*b*) The presentation of original contributions by members and invited guests which are duly scheduled on the annual program. Contributions from nonmembers shall be given a

place on the annual program only when the authors of these contributions have been invited by the Program Committee to participate in the scientific sessions.

The order of the executive sessions shall be—

FIRST SESSION

a. Reading of minutes of previous meeting.
b. Reading of Treasurer's report.
c. Report of Council making recommendations adopted at its annual meeting.
d. Balloting for membership.
f. Appointment of auditing committee.
e. Appointment of nominating committee.

SECOND SESSION

a. Regrets of members unable to attend the meeting.
b. Communications received by the secretary.
c. Action on the death of members during the current year.
d. Report of nominating committee.
e. Election of officers for ensuing year.

THIRD SESSION

a. Report of the editor of the Transactions.
b. Statistical report of secretary.
c. Report of auditing committee.
d. Proposal of new members.
e. Unfinished business.
f. New business.

III. *Parliamentary Procedure.*—Parliamentary procedure at all meetings shall be determined in accordance with the rules of Cushing's Manual.

IV. *Election to Membership and Qualifications for Election.*—Candidates for election to active membership must fulfill the following requirements:

1. The candidate shall have had an internship of at least twelve months in a general hospital approved for internship by the American Medical Association, or its equivalent.

2. He shall have had an internship of at least one year in Neurology in a special hospital for nervous disease or in a special neurological service of a general hospital recognized by the American Medical Association for residence in the specialties.

3. He shall have had one year in Psychiatry in residence in a recognized hospital for mental diseases, or its equivalent in the opinion of the Council.

4. He shall have had a minimum of six months of full time or one year of half time study of neuro-anatomy, neuropathology and neurophysiology.

5. He shall have had five years of active, official service in an accredited neurological or psychiatric hospital or outpatient department.

(These preliminary qualifications shall not go into effect until 1937.)

6. He shall have published four or more articles on neurological subjects in a standard neurological or psychiatric journal.

The Council may in special circumstances waive any or all of the requirements in the case of a candidate who has shown exceptional qualifications or attained recognition in the field of neurology, neurological surgery or psychiatry.

In considering candidates for active membership who have fulfilled these requirements, the Council shall give particular attention to the scientific literary contributions which the candidate has made to neurological or psychiatric literature and shall take into serious consideration the probable continuance of such contributions.

Under certain circumstances the incumbency of important teaching or clinical positions in schools of medicine shall provide justification for election to active membership and the attainment of a position of clinical distinction shall also properly qualify candidates who shall have fulfilled the preliminary requirements for membership.

Nominations for Honorary, Active and Associate membership must be made in writing at the annual meeting of the Association. Nominations of candidates for Honorary Membership shall be signed by six members of the Association; for Associate Membership by five members and candidates for Active Membership shall be proposed by two members and seconded by three members of the Association. Letters of Recommendation shall be written to the Council by the proposers and seconders of candidates for Honorary, Active and Associate Membership. The list of names of all current candidates proposed for election to the Association shall be read at the third Executive Session of the annual meeting.

Candidates for election to Honorary Membership shall possess the usual qualifications prerequisite for such distinction. Candidates for transfer to Senior Membership in the Association shall be 65 years of age and shall have been active members of the Association for twenty-five years. Active members possessing these qualifications shall be automatically advanced to Senior Membership. Active members not possessing these qualifications may be transferred to Senior Membership on recommendation of the Council for reasons deemed sufficient by the Executive Session. Transfer to Senior Membership shall relieve the member from the payment of all dues and assessments and shall allow him the right to vote and hold office in the Association. Candidates for Associate Membership shall be those whose chief professional interests are manifested in lines not distinctly clinical in character but allied to neurology such as neuro-anatomy, neurophysiology, etc.

No officer of the Association shall sign a nomination for membership.

Each candidate shall submit to the Council at least two months before its annual meeting a thesis which shall be carefully examined by a member of the Council and a report thereon made to the Council. Each candidate for active membership shall be assigned to a member of the Council for careful investigation as to his personal and professional qualifications. The Council shall have the power to request from any member of the association a careful and unbiased investigation of the qualifications of any candidate for election to the association.

At least one month before the annual winter meeting of the Council the Secretary shall send to each member of the Association a list of all nominees for election and in the case of nominees for active membership, a printed summary of their qualifications including educational attainments, professional positions and publications. A printed ballot of the names of the nominees shall accompany this list of qualifications, together with a request that each member of the Association shall indicate whether he is in favor of or opposed to the candidate's election. The Council at its annual winter meeting shall, after full discussion of the qualifications of each candidate and a consideration of the ballots and letters returned by the members recommend such nominees as seem most desirable. No candidate for membership shall be voted on at any Executive Session of the Association unless recommended by a majority of the Council.

The candidate recommended by the Council shall be voted on by ballot at the next succeeding annual meeting of the Association. An affirmative vote of two thirds of the members present shall be necessary for election to active membership; an affirmative vote of five sixths of the members present shall be necessary for election to associate membership; and a unanimous vote of the members present shall be necessary for election to honorary membership.

The name of a candidate having once been duly placed in nomination shall remain on the list of nominees from year to year until it has been finally acted upon by the Council or withdrawn by his nominators.

V. *Amendments to the By-Laws.*—On motion, these by-laws, or any one or more of them, may be amended or repealed or suspended by a two thirds vote of all the members present at any executive session during an annual meeting, provided notice in writing of any proposed amendment, repeal or suspension has been given in advance in the executive session immediately preceding the one at which the motion is presented.

News and Comment

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

The fourteenth annual meeting of the Association for Research in Nervous and Mental Disease will be held on Dec. 28 and 29, 1933, at the Hotel Commodore, New York City. The subject to be considered is "The Biology of the Individual." The program will be as follows:

First Day: Morning Session, 9 a. m.

1. Historical Aspects of Individuality and Constitution. Dr. Smith Ely Jelliffe, New York.

2. Body-Build and Its Inheritance. Dr. Charles B. Davenport, Cold Spring Harbor, N. Y.

3. The Rôle of Physico-Chemical Environment in Structural and Functional Expression. Dr. Charles R. Stockard, New York.

4. The Conditioned Reflex in Different Constitutional Types of Dogs. Dr. William T. James and Dr. O. D. Anderson, New York.

5. The Progress of Physical Maturity and Mental Expansion in Childhood. Dr. T. Wingate Todd, Cleveland.

Afternoon Session, 2 p. m.

6. The Ontogenetic Patterning of Infant Behavior. Dr. Arnold Gesell, New Haven, Conn.

7. Constitution and Internal Medicine. Dr. Lewellys F. Barker, Baltimore.

8. Endocrine Types of Constitution. Dr. Walter Timme, New York.

9. Biochemical Aspects of Constitution. Dr. Max Goldzieher, Brooklyn.

Second Day, Morning Session, 9 a. m.

10. Constitutional Aspects of Personality Types with Special Consideration of the Cycloid and Schizoid. Dr. Eugen Kahn, New Haven, Conn.

11. The Eidetic Type. Dr. Heinrich Klüver, Chicago.

12. Personality and the Psychoses. Dr. C. Macfie Campbell and Dr. Karl M. Bowman, Boston.

13. The Schizophrenic Personality with Special Regard to Psychometric and Organic Concomitants. Dr. R. G. Hoskins and Mr. E. Morton Jellinek, Boston.

Afternoon Session, 2 p. m.

14. Individuals and Their Human Environment (Society). Dr. Floyd H. Allport, Syracuse, N. Y.

15. Crime and the Individual. Dr. William Healy, Boston.

16. Personality in the Light of Psychoanalysis. Dr. Paul Schilder, New York.

17. Personality Concept in Relation to Graphology and the Rohrschach Test. Dr. Oskar Diethelm, Baltimore.

18. Constitutional Factors in Psychosexual Development: Their Relation to Personality Disorders. Dr. George W. Henry, White Plains, N. Y.

COLLECTED WORK TO BE DEDICATED TO PROFESSOR HEYMANOVICH

The twenty-fifth anniversary of the medical, scientific and public activities of Prof. A. J. Heymanovich will be celebrated in Kharkov with the termination of the current year, and a special collected work devoted to him will be published. The organization committee for the celebration desires to make this work worthy of Professor Heymanovich and appeals to world experts in neurology and psychiatry to send articles for it. These articles should be sent in care of the Library of the Psychoneurological Academy, K. Liebknecht str. 4, Kharkov (Ukraine), U. S. S. R.

Professor Heymanovich is vice-president of the Ukrainian Psychoneurological Academy and is an active member of the Bureau of the Ukrainian Association for Cultural and Intellectual Relations with Foreign Countries and of the Organization Committee for International Psychoneurological Congresses. He is the author of numerous works in the domain of psychoneurology and has done much to instruct a whole generation of specialists in neurology.

Abstracts from Current Literature

THE PSYCHOLOGY OF DELINQUENCY. GRACE W. PAILTHORPE, Medical Research Council, Spec. Rep. Ser., no. 170, London, His Majesty's Stationery Office, 1932.

This monograph on the psychology of delinquency is sufficiently important to be abstracted in detail. It is divided into six sections: I. Introduction; II. Report on an Investigation into the Psychology of Criminals, 1923-1927; III. Report on an Investigation into the Psychology of Inmates of Preventive and Rescue Homes; IV. Comparisons Between Prison and Preventive Home Cases; V. The Psychopathic Group; VI. Summary and Proposals for a Constructive Policy.

In the preamble Pailthorpe, after discussing briefly the history of the psychologic approach to the study of criminals, draws attention to the presence of two distinct trends in criminology—the sociologic and the biologic—and to the paramount importance of differentiating between these two interests lest confusion result and research be vitiated.

As the sociologist was the first to enter this field of inquiry, it has not unnaturally become the custom to think of the delinquent primarily as a social failure, and always to attribute to him some form of defect, whether intellectual or moral. But if the problem is approached from the standpoint of psychology as a province of biology, it is clear that a comparative valuation is not applicable, and that the criteria to be used must be those of biologic life generally; in other words, success or failure of the individual life. Therefore, the author had to classify the cases into groups from a strictly individualistic point of view, with regard to individual make-up, including intellectual and sentimental capacities and social environment. If we anticipate a little, it will be seen that a large group of criminals was comprised of persons who from the biologic point of view showed a complete and satisfactory adaptation to the form of life which they followed; they were in themselves successful and satisfied, and this psychologic equilibrium was supported by the fact that few of them showed evidence of debility or disease as compared with personalities that were not harmonized.

Section II deals with a study of one hundred prisoners (all women between the ages of 16 and 30). They were studied by the method of personal interview, supplemented and amplified by psychologic tests. Sixty-four per cent of the subjects were of normal and 36 per cent of subnormal intelligence. This confutes the common opinion that persons become criminals because they are subnormal intellectually. It would be much nearer the truth to say that persons become criminals through a defect in the development of sentiments. However, the group of 36 per cent who were subnormal was made up of: those of subnormal intelligence, 21, and those of defective intelligence, 15. Of those who were mentally deficient, in every case, with one exception in which mental conflict was also a strong factor, deficiency in intelligence was the most potent factor in giving rise to delinquency. In the group of subnormal persons, other factors played an important, if not a primary, part, and the subnormality can be looked on as subsidiary.

In 61 per cent of the 64 per cent whose intelligence was normal, the development of sentiments was rudimentary, and in 23 per cent there was some development of sentiments, although it by no means equaled that of the average person; that is, 84 per cent of the total were deficient in the development of sentiments. The remaining 16 per cent were average in the development of sentiments; their cases were those of accidental and psychopathic nature. Of the 61 per cent of patients showing rudimentary sentiment, the egoistic sentiment was present in varying degrees, while other sentiments of patriotism, religion, family, estheticism and altruism were rudimentary or almost completely absent.

In connection with this study of deficiency in the development of sentiments in so large a proportion of cases, the following consideration is worth noting: All the subjects tested, with the exception of two, had been trained in elementary school (or its equivalent). Only seven passed on to any higher form of education by the result of their own efforts. An analysis of these shows: mental conflict, five cases; mental conflict and psychotic trends, one case; mental conflict and epilepsy, one case. Thus the seven cases belong in the psychopathic group.

The figures indicate that a higher development of sentiments was found in conjunction with a greater difficulty in adjustment to reality, that the greater development of sentiments was probably brought about largely because of satisfactory conditions at home and because of the greater degree of intelligence.

When the degree of development of sentiments was contrasted in patients showing mental conflict, the following figures were found:

Development of Sentiments	No.	Mental Conflict	Percentage of Mental Conflict
Rudimentary	61	19	31.0
Developing	22	18	88.8
Average	10	7	70.0

The enormous increase of mental conflict in the patients showing developing and average sentiment is a sign that there is greater evolution or growth in persons of this sort, who are more in touch with reality, than in patients who show only rudimentary sentiment. The person who is widening her personality by the identification of herself with her surroundings will encounter obstacles, some of which will be surmountable and some insurmountable; the insurmountable objects will arouse mental conflict. What stirs one person more than another to reach a higher level of civilization may be due to a multiplicity of factors. That she is unable to reach her ego-ideal is evident in the presence of conflict. What prevents her from reaching her ego-ideal is a matter for analysis: the analysis of a mental and emotional life going on within her of which she is unaware. The adapted person has solved her problem by remaining happily where she is, at an infantile level of behavior, i. e., instinctive, and she reacts like a child in the nursery. The normal adult is also adapted at an adult level of behavior; she has adapted herself to the ways of her own social group and respects the demands on her of the community as a whole.

The adapted and infantile criminal is not even reconciled to her own social group; she refuses to recognize any social group. It is true that she may belong to a gang, but its existence is dependent on this antisocial attitude. The unadapted person is one who has difficulty in adapting herself to her own social group or to the community as a whole, but, in addition, she cannot adapt herself to the "criminal" group in which she finds herself. She has nothing in common with them. True, she wishes to be adapted to her social group, but she cannot achieve this aim.

Forty-four patients showed mental conflict. All of these persons showed shame and self-reproach, projection or negativism: Shame was present in thirty-three cases, projection in twenty-one and negativism in ten. The relative absence of vicious homes was noticeable.

The development of sentiments was average in nine cases, developing in fifteen and rudimentary in twenty. With reasonably good conditions at home there is an increasing number of cases of mental conflict. In other words, persons suffering from mental conflict are those who have attempted to reach a higher standard of development than the others, of whom the majority belong in the adapted group.

Eight cases were psychotic. Thirty-nine per cent of the cases were classified in the biologically adapted group. The subjects were without exception lacking

in development of sentiments. The reality-principle, this term being used in the freudian sense, had not come into play to any extent. These persons are as nearly without apparent signs of repression as it is possible for the human animal to be when he is living with his fellows. As they have no apparent mental conflict, they are more or less adapted; that is, they are successful as biologic units, though failures from the social standpoint. They are not so much psychopathic as sociopathic. These girls were for the most part physically fit and robust. The question arises as to whether these subjects are more capable of profiting by education than the intellectually defective persons. If they were harmonized, could one upset the balance and force them to readapt themselves to a new set of circumstances more in accord with society's demands? Could a certain proportion of them be stimulated to a higher level of sociability by aiming directly at focusing their attention on the gain of deferred pleasure and at the same time applying, indirectly, pain or that which is unpleasurable? In any case, even if a large proportion of this group should be found to be uneducable in this way, they might, possibly, be made useful and productive enough to be self-supporting, if permanently supervised.

Section III is a similar study of one hundred girls who were in seven preventive and rescue homes. The behavior was classified as follows: pilfering, twenty-five cases; sex irregularities, twenty-nine; asocial behavior, fourteen; general subnormality of personality, thirty; unsatisfactory conditions at home, twenty-four; bad companions, two. The conditions at home were classed as: satisfactory, fifty cases; unsatisfactory, forty-one; vicious, nine. In the fifty satisfactory homes the following conditions were found: (*a*) Five of the girls had stepmothers. (*b*) In eleven homes one or both parents were missing; in three, the mother died before the child was 7; in three, the mother died before the child was 13; in two, the father died before the child was 7; in two, the father died before the child was 13; there was one family in which both parents were dead before the child was 13. (*c*) In three cases there were foster-parents from infancy; in two of these instances the child was illegitimate and subnormal in intelligence, and in one, the child was mentally defective.

The chief point of interest in the forty-one unsatisfactory homes was the comparative absence of any kind of parental love in the lives of the children. This, of course, was more pronounced in the vicious homes, and when the figures for unsatisfactory and vicious homes are considered together, 50 per cent of the one hundred girls were brought up on a soil and in an atmosphere where the love found ordinarily in family life was absent. As to intelligence, forty-eight had an intelligence quotient of 75 or over; forty-eight, from 50 to 75, and four, under 50. This means that 52 per cent of the subjects were under par in intelligence, which is of interest when one considers the subjects in prison, only 36 per cent of whom were subnormal.

In this group, the development of sentiments was rudimentary in thirty-five cases, intermediate in forty-eight and normal in seventeen.

In section V the author describes in detail the psychopathic cases. After summarizing her study, the author makes certain proposals for a constructive policy for delinquents. Such a policy is discussed under various heads: (1) education to make the public realize that sudden changes in a child's character are as much an indication of ill health as is a feverish attack; (2) concentration on the investigation of the human beings who are potentially most valuable. Interestingly enough, the potentially least valuable persons are already far more studied and catered to than the others.

Four methods of dealing with the offenders suggest themselves: (1) segregation: (*a*) permanent, (*b*) temporary; (2) permanent supervision without loss of freedom; (3) education; (4) psychotherapy. The subjects coming under headings 1 and 2 would, *ipso facto,* be incurable from the point of view of making them normal social units, but the treatment would render them innocuous to their fellows, or as nearly so in the case of those in class 2 as to render them tolerable. Those coming under headings 3 and 4 are questionably remediable, but, until tested by these methods, they should not be relegated to classes 1 and 2.

Class 1: In this group would be: mentally deficient and subnormal persons of the truculent type; those suffering from the psychoses, and the failures from classes 3 and 4. The first of these subjects will never become amenable to society's demands. That those suffering from psychoses of a certain intensity need either permanent or temporary segregation is obvious, but undoubtedly there are many who are dangerous to others, but who, as conditions stand at present, are not certifiable. Legal recognition of these cases is needed. Persons with incipient dementia praecox, cyclothymic states and paranoid reactions are mentally sick and need treatment in a hospital both for themselves and for the protection of others. Legal recognition of these conditions would mean that every recidivist, without exception, would as a routine be given a full medical examination, physical as well as mental.

Class 2: This group also will be composed mainly of: (*a*) the mentally defective and subnormal persons who are almost mentally deficient, and (*b*) the failures from classes 3 and 4. The type of mentally deficient person in this class is the opposite of the truculent type previously mentioned. The chief danger lies in their submissive disposition. They are quiet, gentle and willing to please, and respond to every suggestion of conduct that is desired of them. Here a permanent supervision outside, which protects the person from harmful external stimuli, will be sufficient. In other words, the environment, if carefully chosen and available, will render the subject innocuous to society.

Class 3: In this class of subjects to be educated should be placed, as an experiment, nearly all of those persons in the adapted group whose intelligence is normal and character not vicious; when formation of sentiments has been slight, and when stimulation toward development of sentiments has been lacking in the upbringing. For them there should be devised a special system of individual training and education. Whether they should be trained in groups under a system of self-government or singly in charge of specially trained women is at present undecided. Both methods should be tried. By education is meant education in social life, as apart from education in branches of work or in the study of lessons.

Since directly or indirectly all accomplishments in life are brought about ultimately through the interaction of loving and being loved, the inhibition of this capacity, either in active or in passive form, is bound to react detrimentally both on the individual and on society as a whole. One of the qualifications, therefore, of those who deal with the education of these young people must lie in the degree of the freedom within them of the capacity to love. It might sound easy to acquire such persons as guardians for these girls, but self-investigation leads to the discovery of how little freedom in this respect the majority of us have.

Failures from this class would, after due trial, be placed in class *a*.

Class 4: This group will include all persons suffering from mental conflict or epilepsy, and those who display psychotic tendencies before a definite psychosis has developed. Full psychologic investigation of the subjects should be undertaken. The investigator would then be in a position to advise: (1) a specialized environment, educative or otherwise; (2) suggestion, direct or indirect, and (3) psychoanalytic treatment. Of cases recorded, there are about 19 per cent in which the use of psychoanalysis is indicated. A trial for a month or six weeks would enable the analyst to know whether it is worth while proceeding with the analysis. A psychoanalytic understanding of the offender should, in any case, put the investigator in possession of the key to the subject's psychology, and then, since every one is not suitable for analysis, other treatment should be advised.

PEARSON, Philadelphia.

OCULAR SYPHILIS. RALPH L. DRAKE, Arch. Ophth. **9**:234 (Feb.) 1933.

The central nervous system is involved in a large percentage of patients in the early stage of syphilis. The involvement may be expressed clinically as symptoms of acute meningitis and of meningo-encephalitis, with papilledema as a conspicuous symptom. Drake discusses papilledema as an expression of acute syphilitic menin-

gitis. He includes an analysis of 50 cases reported and a detailed account of 1 typical case. He thinks that while acute syphilitic meningitis and meningo-encephalitis are relatively rare, papilledema is the most common objective symptom in these cases. It may occur in the three following stages of syphilitic infection: most commonly during the secondary stage, either before, during or soon after the secondary exanthem; much less commonly in congenital syphilis, and in latent periods during the tertiary stage of acquired syphilis.

In a brief abstract of the literature Drake notes that Carr found 12 cases of ocular syphilis in 530 syphilitic patients. Nonne reported 5 cases. Hutinel reported a case in a child aged 3. Mazzeo reported 4 cases in infants between the ages of 5 and 24 months. Ström-Olsen described a case in a patient with juvenile dementia paralytica. Vasiliu reported 3 cases in children whose conditions had previously been diagnosed as tuberculous meningitis.

The pathology according to Jakob is discussed. This form of meningitis is characterized by a diffuse, small cell infiltration of the pia-arachnoid. The inflammation occurs around the blood vessels for the most part, producing infiltration, with intimal proliferation and inflammatory changes, but without degeneration. The brain stem, the circumference of the spinal cord and, not uncommonly, the cerebral and cerebellar convexities are involved, as well as the ventricles. There is frequently a penetration of the exudative process into the marginal zones of nerve tissue, with the formation of encephalitic areas. Spirochetes are not always found.

The symptomatology of acute syphilitic meningitis is unusual and distinctive. The disease may begin abruptly or gradually and is always ushered in by headaches, which diminish and then become worse. The usual symptoms of cerebral meningitis are present: nausea and vomiting, a slight fever, cerebral rigidity, pathologic reflexes and a Kernig sign. Generalized convulsions are not common and occur for the most part in children. Diplopia is often present; aphasia, when present, is usually transient. The pupils usually show abnormalities. The Argyll Robertson pupil was found in approximately one fourth of the cases. The papilledema and papillitis are usually bilateral and occur in degrees of from 2 to 5 diopters; they are accompanied by choroiditis and retinitis. The fields of vision show concentric contraction for form and for color. Of the cranial nerves, the third, fourth, seventh and eighth are most commonly involved; the involvement is more often unilateral and is more pronounced in patients with concomitant meningo-encephalitis. Delirium or coma occurs in some instances; the delirium varies from a mild depression to an acute mania.

The serologic findings in syphilitic meningitis are of the utmost importance. The Wassermann reaction of the blood is positive in about 85 or 90 per cent of cases. The Wassermann reaction of the cerebrospinal fluid is positive in 100 per cent of cases. If the Wassermann reaction of the cerebrospinal fluid is negative on several successive examinations, a diagnosis of acute syphilitic meningitis is probably incorrect. Polleri reported a case, however, in which tests with both blood and cerebrospinal fluid gave negative results; the patient recovered following antisyphilitic therapy. The manometric pressure of the cerebrospinal fluid is slightly increased in the majority of cases. The fluid varies in appearance from clear to turbid and faintly yellow, and usually contains a clot of fibrin. The number of cells in the cerebrospinal fluid is always increased; the cells are largely or entirely lymphocytic; polymorphonuclear cells, however, may be present early in the disease in the more severe cases. The total number of cells varies from 10 to 1,500 per cubic millimeter. The amount of protein is always increased. The chlorides and sugar content may be normal or slightly decreased. The colloidal gold curve, which is not constant, may be of the type found in syphilis or dementia paralytica. Spirochaeta pallida has been found in the cerebrospinal fluid.

Drake states that the prognosis is good if a diagnosis is made early and if antisyphilitic therapy is instituted at once. However, certain cases in which the symptoms were mild are cited in which the patients died after antisyphilitic therapy. Of the 50 cases reviewed from the literature, 40 occurred in male patients, the youngest being 1 year and the eldest 59 years of age. The mortality was more

than 22 per cent. Papillitis was reported in 8 of the 50 patients, and papilledema in 16; the papilledema was bilateral in 14 patients and unilateral in only 2. Unfortunately, in 20 cases no examination of the fundus had been made. Some observers believe that there has been an increase in the incidence of syphilitic meningitis since the advent of arsphenamine therapy; it is believed that the so-called neurorecidive is responsible for acute syphilitic meningitis. Pfister reported six cases following insufficient arsphenamine therapy. The following table lists the outstanding symptoms and their incidence in the 50 patients studied.

Incidence of Symptoms in Patients Studied

Headache	46
Nausea and vomiting	19
Mental disturbances	5
Disturbances of consciousness	13
Fever	18
Paralysis of the cranial nerve	24
Convulsions	4
Visual disturbances	8
Cervical rigidity	35
Kernig sign	10
Babinski sign	6
Aphasia	3
Hemiparesis	2

The typical case described in detail fits well with the symptoms outlined. The symptoms started with failing vision, weakness of the left side of the face, tinnitus and impairment of hearing in the left ear and paralysis of the left abducens. The patient had bilateral papilledema of 2 diopters, which was more marked on the right, without hemorrhages and without exudates. One month after treatment she made a complete and uneventful recovery. Treatment consisted of the administration of potassium iodide, of twelve consecutive doses of soluble bismuth in oil, and of neoarsphenamine, intravenous injection of sodium iodide and drainage of the spinal canal. The total period during which treatment was carried out was eight months.

In summary, the author emphasizes: (1) that while acute syphilitic meningitis and meningo-encephaltis are relatively rare, the possibility of their presence should be considered in any patient showing signs of meningeal involvement; (2) that papilledema is an important clinical sign in this disease and should be sought in all cases, and (3) that the ocular symptoms respond well to antisyphilitic treatment, though in some cases a postneuritic atrophy remains. Drake does not think that a neurorecidive reaction plays any part in the development.

SPAETH, Philadelphia.

PATHOLOGY OF THE NEUROGLIA. EUGEN POLLAK, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **34**:266, 1932.

The glia is a netlike system made up of plasma-poor elements which, depending on location, form a more or less continuous netlike prolongation the surface boundaries of which are the membrana limitans superficialis, the membranae perivasculares and the ependyma of the ventricular system. Depending on the proximity of the network to these surface boundaries, it is constantly undergoing transformation into fibrous territories. Such transformation can occur only by a morphologic alteration of the plasmatic network or by a partial invasion of the glia fibers. The gray matter of the neuraxis is actually the terrain of the small glia belonging to the various types of oligodendroglia, and partly also of the reserve cell elements which, as nucleoplasmatic undifferentiated structures, are ready for any demands that may be made on them by the tissues, either by apposition of plasma in the further differentiation of the nucleus for the purpose of reenforcing the macroglial net or by quantitative division to increase the number of functionally capable glial elements. Except for the reserve cells, the entire glial network, with its relatively rigid structure, represents a type of canal

system not unlike that of the circulatory apparatus, i.e., a communicating system from the arterial limb to the tissues as well as to the venous limb from the tissues. Independently of this network there exists also another glial element, the microglia, which, so far as is known, bears no relation to the macroglia, but represents a second structure which supports the activity of the stabile syncytium and which, owing to its loose connection with the latter, is capable of releasing it whenever it may become necessary to set it into functional activity.

Whereas the function of nerve tissue is limited to specific neural activity, that of the glia is supportive and protective to the parenchyma of the nerve. The neuroglia, then, acts as a provider of nutrition under the most ideal conditions to the nerve cells at the same time that it acts as a scavenger for the removal of substances deleterious to them. In this sense the neuroglia may be regarded as "hermaphrodite," for genetically, as an ectodermal product, it is closely related to nerve tissue, and functionally it represents a medium between nerve substance and connective tissue, possessing certain mesodermal functional properties. In addition to this, the glia also serves as a regulator of the constancy of volume and consistency of the cerebral mass; it tends to equalize whatever variations may occur as a result of cerebral activity. Owing to this property, the neuroglia regulates to a great extent the water content of the brain, which aside from its significance in metabolism in general plays an important rôle in the proper functioning of the entire nervous system.

Three types of pathologic reaction of the neuroglia may be observed in disease of the nervous system: (1) the hyperplastic defense reaction, which is concerned with the maintenance of nutrition of the macroglial and microglial apparatus as well as with its protection against injury; (2) the destructive reaction, which is the result of a disturbance in function of the normal glial structure from the disintegration of tissue and dissolution of the stable elements and their transformation into mobile elements which take care of the destruction and chemical elaboration of the products of disintegration and their removal and transportation into the general circulation; (3) the reparative reaction, which is merely a substitute function that, owing to the functional inferiority of the glia as contrasted with the parenchyma of the nerve proper, produces only scar formation.

Under certain abnormal conditions the neuroglia itself may become diseased. Such a primary condition of the glia is encountered in the form described by Alzheimer as ameboid involvement, which Pollak believes is identical with what he designates as the dysplastic form and Cajal as clasmatodendrosis. This condition is characterized by pyknotic changes in the nuclei, swelling of the plasma and droplike dissolution of the cells. It is also noteworthy that these changes in the glia may run parallel with changes in the parenchyma of the nerve or they may be manifested long before morphologic evidences of parenchymatous involvement are demonstrable. In many cases, especially intoxications (arsphenamine), a selective degenerative disease of the glia may occur in which the latter, in the course of its activity as a filter of the toxic products, loses its defensive power and succumbs before the parenchyma has been affected by the poison. Similar conditions may also be observed in severe circulatory disturbances due to chronic changes in the walls of the cerebral vessels. In these cases the changes in the permeability of the walls of the vessels produce disturbances in the nutrition of the tissue with secondary paralysis of the neuroglia characterized by regressive changes at the height of the hyperplasia of the glial system.

Some observers consider Alzheimer's ameboid glia a postmortem alteration. Pollak does not agree with this view. He believes that, agonally, the nerve cells succumb before the more resistant neuroglia, and that with the death of the cells there occurs in the neuroglia an initial hyperplastic reaction characterized by a swelling of its plasmatic structure. In this stage the neuroglia itself dies from lack of vital nutrition, with resulting degeneration of the cellular process. Although there may occur under certain pathologic conditions a destruction of glia cells, especially in the hyperplastic phase, nevertheless, they keep on functioning as scavengers in their attempt to remove the products of disintegration of the

nerve cells. This theory is offered by Pollak as a possible explanation of the morphologic identity of postmortem and intravital ameboidism.

According to Pollak, disease of the neuroglia plays an important rôle in Wilson's disease and in pseudosclerosis. He believes that the neuroglial changes in these two conditions are due to a hepatogenic disturbance of the water content of the brain. Owing to this disturbance, the capacity of the glia to react with hyperplasia becomes markedly insufficient, so that instead of polymorphous hyperplasia there occurs a luxurious swelling of individual cells or nuclei in which evidences of an aleration in the intracellular water content can be observed. Disturbances of the water content in the glia cells may also be manifested in a different manner. Thus, Alzheimer observed long ago that under certain pathologic conditions the glial network disintegrates into peculiar droplike bodies, producing a mosaic-like formation which he designated as filling bodies. More recently, Holzer has studied these filling bodies and concludes that they are the products of disintegration of the glia fibers. Here one is apparently dealing with a swollen glial formation to which there has been superadded a coagulation of the plasmatic or of the fibrous portions of the glial net resulting from a peculiar combination with water, which leads eventually to a segmental dissolution of the network. It is noteworthy that such peculiar formations are also observed in foci of multiple sclerosis, in which there has occurred hyperactivity of the fascicular glia. The possible significance of such a coagulation process for scar formation in multiple sclerosis is obvious.

KESCHNER, New York.

A FEW REPRESENTATIVE CASES OF PYROMANIA. GEORGE L. WARNER, Psychiat. Quart. **6**:675 (Oct.) 1932.

Limiting the term "pyromania" to an impulse to set fire to buildings without conscious motivation, Warner groups the disorder into two classes, impulsive and compulsive. Behavior of the former pattern is accomplished unexpectedly, without reflection, hastily and without regard to the safety of others or the escape of the pyromaniac. Compulsive behavior is the end-result of a struggle between the patient's intelligence and will, on the one hand, and some irresistible impulse on the other. Effort to resist the impulse results in anxiety, while execution of the act brings relief. The neurosis is seen most commonly in young persons who find themselves in an intolerable situation. Three cases are cited, the pyromania being in one a substitute for masturbation, in the second a symbol of revolt against parental authority and in the third an expression of a subconscious desire to return to the mother.

In the first instance a boy, aged 18, would set fire to baby carriages in apartment house hallways. The boy had been the baby of a large family, having been born when his youngest sibling was 12 years of age. He had been mothered by the oldest sister, who married when he was 7, and whose children were subsequently cared for by him. At the age of 17, he was accosted one night by a man, who borrowed a match from him in the vestibule of an apartment house, and subsequently committed a homosexual assault on him in the same place. The boy then attended a series of dances, and on the way home he would stop in apartment house hallways and set fire to empty baby carriages there. The effort to resist the impulse would lead to anxiety, while its execution was attended by relief. It is significant that about a month before he began the series of arsons, he had stopped masturbating; cessation of this practice had placed him under considerable tension, a feeling similar to the anxiety he felt when resisting the temptation to start a fire. The impulse to set fire to a building always and only followed a dance, when his sexual tension was considerable. It appears that in this instance, arson had been substituted for and had taken on all the attributes of masturbation. It is possible that his resentment against children because they took his mother surrogate (his sister) from him, had some relation to the selection of baby carriages as the kindling point. Undoubtedly his homosexual experience in the vestibule, associated

as it was with the lighting of a match, had something to do with the nature of the compulsion.

In the second instance, a man, aged 28, who had been twice married, would find employment on the estates of rich or prominent men and would subsequently fire the buildings. The motive of anxiety and relief existed here as in most cases. This patient had been reared by aunts and a grandfather on a large estate in Ireland, where he was unhappy because of the stringency of the discipline. At the age of 16, he joined the Sinn Feiners and took part in raids on the estates of British sympathizers, in which arson was a feature. This man had two unhappy marital experiences, and it seems probable that at the conclusion of each his search for and finding employment on large estates represented a desire to return to his childhood home. At these positions he felt, often consciously, that he should have been an heir rather than an employee. The pyromania was a blind striking out against authority (his grandfather, then his employer) which had thus deprived him of his rights. The fact that the attack was by fire was conditioned by his experiences in the Irish rebellion.

A man, aged 31, an illegitimate child, had been abused by his father and protected by his mother. When he was 4 years old, the tenement in which they lived caught fire, and he was rescued by his mother. This experience often recurred to him in dreams. His heterosexual experiences were few, and always both in fact and in fantasy were with older women. He had set fire to several small objects and would masturbate during the fire; he then would feel so much relief that he could extinguish the fire readily. One night he had a strong compulsion to enter the open window of a dark house, did so, and under the excitement of the situation masturbated. He had had several dreams in which, during the act of sexual intercourse, a fire had occurred and his consort had carried him to safety. The similarity between this dream and the experience at the age of 4 seems obvious. Warner believes that the entire life history of this patient shows clearly a desire to return to the mother; the entering through an open window into a darkened room and masturbating there probably represent the same urge. The selection of older women as sexual consorts and the accompaniment of sexual experience with fantasies or dreams of fire point to the same mechanism.

A fourth instance of pyromania, in a schizophrenic person, is given, but the motivations are less clearly established.

DAVIDSON, Newark, N. J.

AN ATTEMPT TO TRANSMIT POLIOMYELITIS TO SPLENECTOMIZED GUINEA-PIGS. HERMAN CHOR, Arch. Path. **15**:387 (March) 1933.

There have been many attempts to discover some animal other than the monkey which might be suitable for experimental studies of poliomyelitis. If this could be done, advances might be made in the knowledge of poliomyelitis comparable to those concerning yellow fever which followed the demonstration by Theiler that white mice can be used as well as monkeys for experimental purposes. Harmon, Shaughnessy and Gordon reported the negative results of repeated efforts to transmit poliomyelitis to animals of many kinds. Chor proceeded in a slightly different manner, for he splenectomized the animals before inoculation. It was thought that removal of the spleen might lower the resistance so that the virus might "take" in animals in which it would not ordinarily do so. There is a considerable amount of evidence that resistance to other infective agents can be decreased in this way. That splenectomy alters the general resistance of the animal was well borne out by the experiments. The daily records of temperature and clinical symptoms and signs showed that the splenectomized guinea-pigs invariably reacted more severely than the unsplenectomized guinea-pigs to the procedures employed. Not one unsplenectomized animal died during the five week period. They were killed for examination. Another noticeable feature was that the splenectomized animals which were inoculated with poliomyelitic virus reacted more severely than those in which injections of an emulsion of normal monkey brain were made. No deaths occurred before five weeks in animals inoculated with pure

emulsion of brain. A rise in temperature and some degree of sluggishness usually followed inoculation with the virus; these symptoms were more outspoken than in the animals inoculated with the pure monkey brain.

Perhaps the most outstanding feature post mortem was lymphoid hyperplasia. The mesenteric lymph nodes, the supraclavicular group, the submental and the inguinal glands were often enlarged to a striking degree. That lymphoid hyperplasia often occurs after splenectomy, as a compensatory mechanism, is well known. The hyperplasia, however, is rarely acute; examination of splenectomized controls failed to show any special enlargement of the lymph nodes. A second consideration is that the introduction of any inoculum into the peritoneal cavity or subcutaneous tissues usually calls forth some lymphatic activity, regardless of the nature of the material used. This was confirmed by the finding of some degree of hyperplasia of the mesenteric nodes in the guinea-pigs inoculated with normal monkey brain.

Splenectomized guinea-pigs do not acquire the nerve lesions characteristic of poliomyelitis following inoculation with potent monkey virus either in direct or in passage experiments. They do show a decrease in resistance to such inoculation, which produces in many a condition characterized by fever, general sluggishness and lymphoid hyperplasia, with death often occurring within fourteen days.

WINKELMAN, Philadelphia.

PATHOLOGY OF AMYOTROPHIC LATERAL SCLEROSIS. A. PEKELSKY, Jahrb. f. Psychiat. u. Neurol. **49**:74, 1933.

Four cases of amyotrophic lateral sclerosis, with a duration of ten months, four years, twenty-six years and three years, respectively, are reported. As the average duration of amyotrophic lateral sclerosis is four years, the case of twenty-six years' duration is noteworthy. In this patient the first symptom was paresis of several months' duration, which was diagnosed as polyneuritis. Recovery from the polyneuritis was never complete; the patient had periodic attacks of pain in the limbs; the final stage developed in an apoplectiform fashion; the changes in the muscles observed at this time could not be attributed to the recent acute process, but must have been developing gradually. The short duration of the disease in the case that lasted ten months is attributed to the relatively early appearance of bulbar manifestations. The clinical course in all cases was that of a typical progressive motor disturbance, which began asymmetrically and gradually affected almost the entire musculature. In two of the cases the bulbar symptoms appeared after the spinal symptoms were advanced, and in another the bulbar and spinal symptoms appeared simultaneously. It seems, also, that in some cases bulbar symptoms may appear in an apoplectiform fashion. In two of the cases severe pains in the limbs were a feature throughout the disease. The cerebrospinal fluid was normal in every case. A correlation of the clinical picture with the histologic findings also confirmed the well established fact that marked structural changes occur in the central nervous system without clinical manifestations.

Relatively speaking, the histologic changes were similar in all cases. Whatever differences there were could be accounted for by the age of the patient and the duration of the disease. It is noteworthy that lesions were observed also in structures adjacent to the pyramidal and anterior horn cell systems, so that the disease apparently is not a pure systemic disease. The lesions were those not only of demyelinization, but also of axonal degeneration, which was observed in the form of scattered patches. There was no evidence of meningitis, meningopathy or radiculitis. The anterior horn cells seemed more affected in the caudal portions of the neuraxis. In the cervical region these elements were preponderantly atrophic and sclerosed, whereas in the lumbar region they showed more lipoid and less sclerotic degeneration. Sclerotic as well as lipoid changes were also observed in the cells in various places in the gray matter of the cord and in the medulla. In some of the cases there were numerous small softenings and

hemorrhages in the vicinity of the degenerated corticospinal tracts. Small foci of softening were observed also in the white matter of the anterior central convolution and in the pons. The author attributes the variations in the clinical picture to the presence of the miliary softenings in various regions near the pyramidal system.

KESCHNER, New York.

OCULAR MOVEMENTS OF DIRECTION AND OF CONVERGENCE. M. MARQUEZ, Ann. d'ocul. **169**:769 (Oct.) 1932.

The motor apparatus of the eye serves the visual function. When an object appears the eyes are directed toward it or away from it. If the eyes are directed exactly toward the object, the image is formed on the fovea centralis of the retina. In this case the extrinsic muscles of the eye do not need to function, but it is necessary for the intrinsic muscles of the eye to produce sufficient accommodation and contraction of the iris to make a clear image of the object examined. If the object is displaced to one side of the visual line a confused image results because it is not formed on the fovea. A reflex act occurs, and the fovea is placed so that rays of light from the object are focused on it. Because the image of the object is formed on the retina and because the anterior and posterior poles of the eye move in an inverse direction to place the fovea in position, it is necessary for the extra-ocular muscles to contract so that the anterior pole of the eye is moved in a direction opposite to that of the retina which receives the impression.

The movements of one eye are similar to those of the other and they must be simultaneous. In lower forms of animal life the visual fields are independent because of the lateral position of the eyeballs and movements of convergence are unnecessary. In higher animals the eyes are directed forward and binocular visual field develops. Although this field is small in certain animals, for example, in rabbits, it is large in other animals, e.g., in the dog and monkey, and is largest in man. When binocular visual field appears the function of convergence also develops, because it is necessary that both eyes be directed to the same point in space at the same time. Movements of convergence in binocular vision are the most recent steps in evolution, and therefore it is the function of convergence which is most frequently disturbed. This is proved by statistics on strabismus.

The disputed question of the fusion of images with noncorresponding points in the retina, suggested by the famous experiments of Wheatstone, which were badly interpreted by him and by many other authors, is briefly discussed. This fact has been demonstrated by others (Hering: *Beitr. z. Physiol.*, 1861-1864, p. 81, and Bourdon: La perception visuelle de l'espace, Paris, 1902, p. 209). Marquez is also convinced that this is possible.

Marquez suggests that a distinction be made between the two types of movements, those of direction and those of distance, in which the two visual lines converge on a point of the object fixed. The study of these two types is not only a question of definition but also of exactness of concept which enables one to differentiate accurately between these two functions. This distinction has been made several times, notably by Hering and Parinaud. Neglect of this study results in error in interpreting normal and pathologic conditions and, in clinical work, in the diagnosis of motor anomalies.

BERENS, New York.

SEXUAL DEVELOPMENT OF BOYS. PAUL E. KUBITSCHEK, J. Nerv. & Ment. Dis. **76**:425 (Nov.) 1932.

Kubitschek aims at the establishment of more definite standards of physiologic sexual development, particularly of the secondary sex characters. He attempts to estimate the relationship between testicular development and the development of secondary sex characters and structural types as well as to correlate, if possible, the sexual development and the personality make-up of the person. Two theories are in opposition on this point: one, that the gonads furnish a direct stimulation and control of the development of the sex characters; the other, that the total

sex characters are more or less preexistent and that the gonads exercise only a protective influence on their actual development.

A study of 730 boys, aged from 9 to 18 years, was undertaken; 125 were Negroes. Male subjects were selected because of the accessibility of the gonads for measurement. The uniformity in the degree of gonadal development in the group of boys aged 9 and 10 years was greater than that in the boys aged 11 and 12 years. Subjects in the group of those aged 13 years were the first to show a period of rapid sexual development. In this group the quality of the voice did not seem to correspond strictly with the development either of secondary sex hair or of the testes. Wide variations in the degree of biologic maturity in the group of those aged 14 and 15 years were also striking, but the maturation process was less rapid in the latter group and became still slower in the groups of those aged 16, 17 and 18 years. Examination of the Negro boys showed as great a variety in the rate of sexual development as did that of the white boys, which fails to confirm the prevalent impression that Negroes and persons of tropical countries mature more rapidly than those of the temperate zones.

Some classification of the personality types of these boys was undertaken according to Kretschmer's division of schizoid, cycloid and mixed categories, but the author was unable to establish any correlation between these and structural types. There was an absolute lack of dominance of any one type of personality in the groups of retarded, average and advanced sexual development.

Kubitschek finds that the secondary sex characters develop at a more uniform rate than the primary characters, and that the development covers a longer period of time. Striking variations between the degrees of development of the primary and secondary sex characters were also encountered, and the impression was gained that insufficiency or dysfunction was of a pluriglandular nature, in which the secondary sex character was dependent on and controlled by the correlated activity of the endocrine system as a whole and not by the hormone furnished by one gland alone. Some relationship was found to exist between structural type and secondary sex characters. Retarded development predominated in asthenic types, while the reverse was true of the athletic and pyknic types.

HART, Greenwich, Conn.

ANGIOMATOUS MALFORMATIONS OF THE BRAIN. VICTOR LEVINE, Arch. Path. **15**:340 (March) 1933.

In the past few years widespread interest has been aroused in the subject of blood vessel tumors of the brain, especially since the publication of the monographs by Lindau, in 1926, and by Cushing and Bailey, in 1928. The latter authors divided these tumors into the hemangioblastomas, which have been dealt with especially by Lindau, and the angiomatous malformations, of which a considerable number of cases have been reported. Because of the relative rarity of vascular malformations of the brain (Cushing and Bailey list 16 cases among a series of 1,522 cases of verified tumors of the brain; Dandy, 16 among a series of 600), it was thought worth while to report 2 cases in both of which the condition was discovered post mortem. These cases occurred in a series of 24 cases of tumors of the brain among 4,100 autopsies.

That angiomas of the type described in this article are not true tumors, but rather angiomatous malformations, is clearly shown in both cases. The distinguishing features are the lack of new formation of blood vessels or of vasiform tissues and the presence of islands of nerve tissue showing gliosis between the vessels. Cushing and Bailey stressed the importance of these islands of nerve tissue in deciding that the malformations are congenital. Most authors, however, fail to mention them. Only the reports of Buckley, Rühl and Stewart and Ashby take cognizance of them. Undoubtedly the malformations occur early in fetal life, since usually, as in these cases, they fit into the brain with little or no displacement of the surrounding tissue. This conception of congenital malformation is favored by the fact that many venous angiomas in children have been described.

Diagnosis of tumors of the type described is often difficult to make during life; many are recognized only at operation. The presence of a facial nevus is suggestive but not by any means indicative of a similar abnormality of the blood vessels of the brain. If a person with a facial nevus has contralateral jacksonian epilepsy or paralysis, a diagnosis of angioma of the brain is probable. Other neurologic symptoms are often present. The presence of a cerebral angioma can often be verified by roentgenologic examination. Twenty-one of the cases recorded in the recent literature occurred in patients with facial nevi. All but 1 of the patients had definite neurologic symptoms; in this patient ocular findings directed attention to the cerebral condition. In 14 of the patients there were typical roentgenologic findings. One diagnosis was verified by an encephalogram while in 4 patients there were only the facial nevus and the neurologic symptoms on which to establish the diagnosis.

WINKELMAN, Philadelphia.

HYSTERICAL OVERLAPPING IN A CASE OF INJURY BY TRACTION OF THE RIGHT BRACHIAL PLEXUS: NEUROTIC SEQUELAE OF ACCIDENTS. P. SCHNYDER, Schweiz. Arch. f. Neurol. u. Psychiat. **28**:293, 1932.

As a paradigm for a thorough discussion of traumatic neurosis, the author presents the history of a classic case. The patient, an ambitious but poorly educated man, had evidently never become reconciled to the necessity of earning his livelihood by manual labor. Following a painful but otherwise trivial injury to the brachial plexus, he was unable, by reason apparently of lack of courage and energy, as well as an undue hypersensitiveness, to prevent ankylosis of the right shoulder joint and atrophy from disuse of the corresponding arm. To the inability to use the right arm were added a right hemihypesthesia and a functional paralysis of the right leg. A desire for compensation, unduly prolonged examinations, neglect of psychotherapeutic measures and the injudicious use of diathermy, the effects of which the patient feared, were, in the author's opinion, important contributing factors in the development of the neurosis. When the author examined the patient several years after the injury, he was surprised to find, instead of an embittered and contentious man, a jovial and courteous man, resigned to his fate and actively engaged in the reading of popular scientific literature, as well as in learning to write with his left hand. The patient declined to submit to the proposed psychotherapeutic measures, but, encouraged by the assurance that his malady was not incurable, he consulted an irregular practitioner and was cured of the functional paralysis by the application of a magic salve.

While admitting the importance of the prospects of compensation in the genesis of traumatic neurosis, the author warns against the unqualified acceptance of the dogma implied by the term "compensation hysteria." In his opinion the condition belongs in the larger group of psychoneuroses, the causes of which are to be found in feelings of inferiority in one desirous of being superior, a deficient sense of social responsibility and a false sense of values. Deficient moral and mental training is probably of greater importance than an inherited psychopathic trend. As a prophylactic measure, Schnyder urges the early resumption of former activities and the prompt institution of psychotherapeutic treatment designed to convince the patient that recovery is more desirable than compensation. Even a well established neurosis is, in the author's opinion, not entirely hopeless from the therapeutic standpoint. An extensive bibliography is appended.

DANIELS, Rochester, Minn.

THE FALSE CLAIMS OF THE PSYCHOANALYST: A REVIEW AND A PROTEST. BERNARD SACHS, Am. J. Psychiat. **12**:725 (Jan.) 1933.

This review of Wittel's book "The Medical Value of Psychoanalysis" takes the form of a full length, original article. Sachs accuses psychoanalysts of hiding behind unintelligible and obscure terms and resents their charge of ignorance and

fear leveled against all who oppose their theories. The contention that the analysts established the unity of man as a psychic and biologic being is an example of impertinent conceit, for this concept existed long before Freud and needs no further demonstration. The interpretations of a psychoanalytic interview can never be demonstrated logically and are often varied when the same patient is subjected to several analyses. The insistence that no man can thoroughly understand a patient's neurosis unless he can live it himself is palpably absurd, and would require a competent psychiatrist himself to have insane trends. Sachs implies that the insistence of the analyst on long periods of daily or almost daily treatment is motivated by commercial influences; this implication is veiled in his phrase: "It is easy to understand why this method is especially fascinating in private practice."

All that the psychoanalytic interview does, Sachs believes, is to teach the patient to "burrow into the supposedly unconscious, and bring forth forgotten and often unimportant experiences . . . giving them an interpretation in accordance with the examiner's own prejudices." One of Freud's primary concepts—the suppression of unpleasant ideas—is rejected by Sachs as contrary to the obvious fact that it is often precisely the humiliating experiences that return again and again to plague us. Sachs is particularly bitter toward the phenomenon of transference, charging that it has wrought untold mischief. In a footnote Sachs deplores the fact that analysts sometimes encourage or even order patients to "violate the prevailing code of morality." Toward analysis of children he is equally bitter, accusing the analyst of upsetting the mental processes of the child; he insists that although "the analyst may continue his nefarious practice with the adult, he must in all seriousness keep his hands off the child." Another feature of the freudian technic that irks Sachs is the absence of adequate records of the interview, a carelessness tolerated in no other branch of medicine. "The whole thing," he charges, "is veiled in suspicious mystery."

Sachs closes the review with the caution that the psychoanalyst is a good salesman, and he warns the medical man "not to fall for the unconscious, infantile sexuality, the Oedipus complex, the interpretation of dreams, the transferences, the projections and what-not." The future of psychiatry must be placed, Sachs believes, in safer and saner hands.

DAVIDSON, Newark, N. J.

BIOCHEMISTRY AND MENTAL DISORDER. J. H. QUASTEL, Lancet **2**:1417 (Dec. 31) 1932.

Mental symptoms accompanying anoxemia produced by ascents to high altitudes are well known. They include loss of memory and judgment, temporal disorientation, irritability and emotional instability. Abnormal mental symptoms accompany or follow carbon monoxide poisoning, and there seems to be little question that anoxemia of the brain may lead to abnormal behavior. Anoxemia, however, is created not only by lack of oxygen, but also by conditions being set up which render the oxygen unavailable for oxidative purposes. Disturbances in the nervous system which result in diminished rates of oxidation, therefore, could be productive of mental disorder. It has been shown that narcotics give rise to severe mental disturbances; they have precisely the property of diminishing the rates of oxidation brought about by the brain. They all specifically inhibit, at low concentrations, the oxidations by brain tissue of substances important in carbohydrate metabolism, viz., dextrose and lactic and pyruvic acids. This inhibition is accomplished in the cases of such drugs as phenobarbital, a phenobarbital derivative and chloretone at concentrations that will bring about deep narcosis. The oxidation of substances such as sodium succinate or *p*-phenylenediamine, which are oxidized freely by the brain, is not affected by narcotics at low concentrations. The results indicate that the narcotics do not interfere with the access of oxygen to the brain cell or with the activation of oxygen by the brain catalysts, but with the mechanisms that result in the activation of lactic acid or pyruvic acid. The narcotics in this way inhibit the rates of oxidation of lactic acid and pyruvic acid. Since it is known that one of the chief sources of energy

to the brain lies in the oxidation of lactic acid, it follows that a narcotic which is absorbed at or is combined with a particular nerve center will diminish the energy supply to this center, and hence will depress its functional activity.

Knowledge that narcotics interfere with carbohydrate metabolism had led to the development of treatment for mental illnesses by narcosis. The danger accompanying this type of treatment lies in the toxic by-effects of the prolonged use of the drugs. It seems probable that the toxic by-effects are linked with the disturbance in carbohydrate metabolism, and this view is supported by the fact that ketonuria often accompanies prolonged treatment with narcotics. It is now being found by Quastel and a co-worker that the toxic symptoms, including ketonuria, are greatly alleviated by administration of dextrose and insulin while the patient is under the influence of the narcotic.

BECK, Buffalo.

PSYCHO-ANALYSIS AND MEDICINE. FRANZ ALEXANDER, Ment. Hyg. **16**:63 (Jan.) 1932.

After reviewing briefly the history of psychoanalysis, Alexander points out that the resistance against it has changed from a stubborn emotinal prejudice to a superficially rationalized intellectual objection to its apparent lack of scientific methodology. Psychoanalysis does not deal with phenomena that can be weighed and measured; yet one cannot close one's eyes to a significant subject matter for this reason. Indeed, psychologic science has an advantage over the objective sciences in one particular at least: The observer is able to appreciate (by introspection) the unexposed thought processes of the subject. He charges behaviorism with a deliberate refusal to use this capacity, with a resulting narrowing of outlook. The psychologic method will rank with objective technics only when certain errors are avoided; for these errors, Alexander sees four sources: (1) unwillingness on the part of the subject to explain his thoughts and motives; (2) inability of the subject because of his ignorance of subconscious psychic mechanisms properly to interpret his behavior; (3) differences between subject and observer that impair rapport, and (4) prejudice on the part of the observer. Alexander believes that these errors are reduced to so trivial a proportion by psychoanalysis as to render psychologic technics truly scientific. Unwillingness on the part of the subject to explain his motivations is rendered unlikely by the patient's desire for relief and help. Inability to understand his own behavior is taken care of by the release and interpretation of uncontrolled free association. The analyst's experience makes it unlikely that the difference between him and his patient will influence his therapy, while didactic analysis sweeps away the emotional prejudice which clouds interpretative psychology of every other sort. The result of the application of this method has been the explanation of previously inexplicable behavior on the part of the neurotic and the psychotic. The paper is closed with the announcement that Freud has created a method whereby language is used, not for hiding thoughts, but for explaining them.

DAVIDSON, Newark, N. J.

A NOTE ON THE OPERATIVE TREATMENT OF FACIAL PALSY. CHARLES BALLANCE, Brit. M. J. **1**:787 (April 30) 1932.

Three operations are reported on baboons in which the facial nerve was divided on one side and at least 3 cm. of the nerve was taken away from the aqueduct of Fallopius to prevent union of the divided ends. An anastomosis with the glossopharyngeal nerve was performed in one case and with the auriculotemporal in another. In a third case, 7 mm. of the facial nerve in the fallopian aqueduct was replaced by 7 mm. of the descendens noni nerve. In the first case recovery was almost complete, but associated movements during swallowing were noticed. In the second case, recovery was even more complete and there were no associated movements. In the third case, rapid and complete recovery from the facial palsy was observed; there were no associated movements and no spontaneous spasm

occurred. The author believes that the graft operation is much to be preferred to any anastomosis possible. Stimulation of the facial area of the rolandic cortex and of the nerves in the posterior fossa of the base of the skull was undertaken as a routine in the final examination of each experimental animal. In the first case, stimulation of the facial area of the rolandic cortex gave a normal response in the muscles of the right side of the face. This also occurred in the other two cases. Stimulation of the right facial nerve in the first case, after the animal had been killed, gave no response. Stimulation of the right glossopharyngeal nerve gave good contraction of the muscles of the upper and lower lips and retraction of the angle of the mouth. With a stronger current, the right eyelid closed. Stimulation of the right glossopharyngeal nerve at the lower border of the jugular foramen caused contraction of all muscles of the right side of the face. In the second case, similar stimulation of the right facial nerve at the base of the skull gave no response and of the right fifth nerve caused contraction of all muscles of the right side of the face. In the graft operation, stimulation of the right and left facial nerves in the posterior fossa, after removal of the brain, produced equal and full contraction of muscles of the right and left sides of the face.

FERGUSON, Niagara Falls, N. Y.

LACUNAR DISINTEGRATION IN THE SENILE CEREBRUM, AND THE PSEUDOBULBAR SYNDROME: A CASE. I. COSTA RODRIGUES and A. BORGES FORTES, An. assist. a psicop., 1931, p. 169.

Costa Rodrigues and Borges Fortes consider the lesions that are frequently found in the brains of aged persons. Lacunar degeneration is characterized by the existence in the cerebral substance of small cavities, with more or less irregular contours, and of small lacunae ranging in size from that of the head of a pin to that of a pea, or even larger. Such lacunar foci are found in varying numbers and are distributed almost exclusively throughout the central portions of the brain or, more exactly, throughout the central gray nuclei, chiefly in the putamen (less frequently in the optic thalamus and in the head of the caudate nucleus), and in the adjacent white substance, notably the internal capsule. The authors describe in detail the case of J. L., a white man, a Spaniard, a laborer, who said he was about 50 years old, but who evidently was much older. He entered the hospital in a state of psychomotor excitation and mental confusion. He admitted later the use of alcoholic beverages, but said that he had not had venereal disease. He did not recall having had any other diseases. The patient died twelve days after admission to the hospital. Macroscopic examination of the nerve centers revealed a slight thickening of the cerebral pia mater. There were no changes of the large vessels pointing to syphilis or arteriosclerosis. Lacunar degeneration was found. There was considerable increase of the perivascular space. The vessels were intact, there being no changes in the walls. Lacunar degeneration was more evident in the putamen, in the substantia innominata and in the external nucleus of the globus pallidus. These lesions were frankly evident in the two hemispheres. In the same cerebral section foci of degeneration were observed in the white substance of the hemisphere, just below the cerebral cortex of the first right ascending frontal convolution. In the section passing through the border of the corpus callosum, there was nothing of moment. Likewise, the section passing through the occipital lobes was in no respects abnormal.

EDITOR'S ABSTRACT.

CONTRIBUTION TO THE NEUROPHYSIOLOGY OF THE URINARY BLADDER IN MAN. JAMES R. LEARMONTH, Brain **54**:147 (June) 1931.

The components of the sympathetic and parasympathetic nerves that pertain to the innervation of the bladder are described. This nerve pathway insures integration of the physiologic processes concerned in the formation and disposal of urine. Intravenous injection of epinephrine caused contraction of the trigonal

region of the ureteral orifice and increased expulsion of urine in a patient with an exstrophic bladder. By means of faradic stimulation, proof is furnished that the trigonal region and internal sphincter are controlled by the sympathetic system, which innervates also the musculature of the prostate, seminal vesicles and ejaculatory ducts. In an analysis of the various impulses carried by the nerves of the bladder, both the sympathetic and the parasympathetic pathways contain afferent impulses giving information as to the degree of distention and painful sensations. Most, if not all, "reflex" afferent fibers from the bladder are conveyed by the parasympathetic pathway. As to the efferent fibers, the parasympathetic supplies the motor fibers for the detrusor muscle, while the inhibitory fibers for the detrusor muscle come from the sympathetic pathway. The latter also contains vasoconstrictor fibers for the vesical blood vessels. The second and third sacral are the most important spinal segments connected with the parasympathetic pathway to the bladder. In the physiology of the component parts of the bladder, the sympathetic influences act as a brake on contractions of the detrusor. The maintenance of closure of the internal vesical sphincter depends on its inherent tonus, which is dependent on the integrity of reflex fibers in the parasympathetic pathway; the latter system is alone essential for the act of micturition.

The author conceives the act of micturition as a modified autonomic reflex the points of stimuli of which are the vesical musculature and the internal vesical sphincter. As in other neurologic concepts, micturition as a pure reflex must be limited to infancy; adult control is a more complete subjugation of an originally primitive spinal function to cerebral influences.

MICHAELS, Boston.

PATHOGENESIS OF RETINITIS PIGMENTOSA. JONAS S. FRIEDENWALD and EUGENE CHAN, Arch. Ophth. **8**:173 (Aug.) 1932.

The article, as it originally appeared, can be of academic interest only to the neurologist. The experimental work, however, brought out various points, which are of interest to the neurologist. Phagocytic activity of the Müller's fiber cells of the retina has not, so far as is known, been previously observed, though phagocytosis by other retinal glia has been reported. Whenever glia cells are found to be phagocytic, the question may be legitimately raised as to whether they are truly epithelial in origin, and whether they may not be related to the microglia of Hortega. In regard to Müller's fibers this can definitely be answered in the negative. According to Mann, Müller's fibers appear in the earliest differentiation of the retinal cells, before the primitive retina is invaded by mesenchyma.

It has been generally believed by neurologists that only glia cells of a mesodermal origin have phagocytic function. From their experiments the authors conclude that no primary retinal lesion outside the neuro-epithelium is necessary to account for the clinical and histologic pictures of this disease. The experiments do not enable them to decide whether in the natural disease both elements of the neuro-epithelium are primarily involved, or whether the disintegration of the rods and cones is secondary to the scattering of pigment from the pigment epithelium, or vice versa. It is interesting, also, that a question may arise as to whether atrophy of the retinal ganglion cells can occur in cases of retinitis pigmentosa sine pigment. It would appear that the degree of atrophy is closely related to the amount and duration of the pigment in the retina.

All the histologic changes in the retina in retinitis pigmentosa can be accounted for on the hypothesis of a primary lesion of the retinal neuro-epithelium, with secondary, long-continued infiltration of the retina by melanin granules.

SPAETH, Philadelphia.

NIRVANOL ERUPTIONS. JOHN F. MADDEN, Arch. Dermat. & Syph. **26**:1065 (Dec.) 1932.

Phenyl-ethyl-hydantoin is becoming increasingly popular in the treatment of chorea, the chief drawback to its more extensive use being the apparently alarming nature of the reaction. This is likened to a serum sickness, with a definite period

of incubation during which amboceptors are produced. At first nirvanol produces an alkalosis which somewhat approaches tetany; this accounts for the temporary aggravation of the choreic movements. At the moment of eruption this changes into an acidosis, and it is probably this sudden alteration which has such a marked effect on the central nervous system. The dosage and duration of treatment with nirvanol recommended by various authorities are surprisingly uniform: 5 grains for younger and 10 for older children in two or three doses a day until the fever or eruption appears. The administration should cease on the twelfth day if by that time there has been no reaction.

The symptoms proceed with clocklike precision. On the second or third day the movements are aggravated; this period is soon followed by the development of sedation; fever appears on the seventh or eighth day, and subsides within the next three days. The cutaneous condition is noticed on the tenth or eleventh day, the lesions first appearing on the chest or abdomen and soon involving the extremities. The face is seldom involved. The lesions are macular, and they enlarge and become elevated. The temperature usually is below 102 F. and seldom above 103 F., and returns to normal shortly after the discontinuance of the drug. The cutaneous lesions fade and eventually disappear entirely without any residual scarring, pigmentation or desquamation. Histologically, the skin resembles any toxic erythema. Complications of sickness due to nirvanol are negligibly few and usually of no serious import.

DAVIDSON, Newark, N. J.

HALLUCINATORY DELIRIUM OF DRINKERS: THREE CASES. O. GALLOTTI, An. assist. a psicop., 1931, p. 43.

Gallotti points out that patients with hallucinatory delirium often continue their usual occupations for weeks. The somatic signs of alcoholism are ordinarily either not present or very slight. Kraepelin held that delirium tremens and hallucinatory delirium of drinkers are not essentially different processes, but represent slightly different forms of the same disease. The duration of hallucinatory delirium in the acute form ranges between a few days and a few weeks. In the subacute form the delirium may be prolonged for three or four months. It is evident that if the patient continues to drink alcoholic beverages, the delirium may recur. A considerable number of the patients, however, do not recover, and in that case a definitive mental debility develops, with psychosensory disturbances and delirious ideas. The chronic evolution begins with changes in the emotions. The patient becomes timid and suspicious and is dominated by a feeling of insecurity. At times he hears voices that make personal allusions or threats. Gradually, the hallucinations increase in number and intensity. If the patient ceases to drink, they diminish considerably, but do not disappear. If the patient relapses in the abuse of alcoholic beverages the same symptoms recur, so that finally even a long abstinence does not prevent auditory hallucinations from manifesting themselves. There arise illusory perceptions of all kinds and fantastic ideas of persecution. Ideas of grandeur may also appear. In speech, neologisms and jumbles of words are observed. In Italy, hallucinatory delirium is more common than delirium tremens, but in Germany and Switzerland the latter is more common.

EDITOR'S ABSTRACT.

CONTRIBUTION TO THE QUESTION OF ACUTE MULTIPLE SCLEROSIS. A. REUTER and R. GAUPP, JR., Ztschr. f. d. ges. Neurol. u. Psychiat. **138**: 495, 1932.

The question of the relation of acute multiple sclerosis to acute encephalomyelitis disseminata is important. Pette considers the two processes identical. Reuter and Gaupp report the case of a man, aged 36, in whom hemiplegia developed within a few hours, which receded in a few days. Ten days after the first symptom was noted edema of the lung appeared. Neurologically there were spastic hemiparesis, nystagmus, ocular palsy and bulbar symptoms. Death occurred nineteen days after the first symptom appeared.

Pathologically there were multiple foci in the nervous system, particularly around the ventricle, in the chiasm and at the junction of the cortex and white matter. Microscopically there were varied pictures. Many foci showed the typical characteristics of multiple sclerosis: loss of myelin sheaths, with more or less intact axis cylinders, and marked proliferation of astrocytes. On the other hand, there were a number of fresh foci with acute proliferation of glia cells, numerous gitter cells and acute inflammatory phenomena. The infiltrating cells were almost exclusively lymphocytes and plasma cells. There was no increase in fibrous glia in these areas and no loss of myelin sheaths. The pathologic picture pointed to an older process than the clinical picture indicated. There were old foci with more recent foci near them. The histologic picture is that of different stages of multiple sclerosis. The acute foci are those of acute multiple sclerosis. Reuter and Gaupp do not think that acute multiple sclerosis and acute encephalomyelitis disseminata are the same process.

ALPERS, Philadelphia.

INTRACRANIAL CALCIFICATIONS: STEREOGRAPHIC STUDY. J. CAMPOS, An. assist. a psicop., 1931, p. 81.

Campos points out that intracranial calcifications may be entirely mute in their symptomatology—mere roentgenographic revelations—or, on the other hand, they may be the cause of more or less grave symptoms, depending on their nature, the primary lesions from which they originate, and, more particularly, their localization with respect to adjacent nerve tissues. Intracranial calcifications may be divided into: (1) those that are in close relation with the cranium, being derived from it, and (2) those that develop at the expense of the soft parts. The former are due to traumas, either primary or metastatic. The osteomas and osteochondromas in their evolution reach the brain, but their intimate relations with the cranium remain evident. These relations are either en masse or by means of pedicles that are closely connected with the bony tissue at the point of departure. Phlebolites, which develop in the vessels of the pacchionian depressions, are also frequently found. The latter (that is, those that originate in the soft parts) develop at the expense of changes in the meninges, the nerve tissues, the blood vessels, the choroid plexuses and the glands. These changes are traumatic, inflammatory, tumoral, degenerative or due to sclerosis of the blood vessels, cysticerci or echinococci. These pathologic processes may, either by their own evolution or by their own curative processes, lead to calcareous deposits, with visibility, by means of roentgenographic aid, of lesions or of their vestiges.

EDITOR'S ABSTRACT.

THE TRYPTOPHAN TEST IN TUBERCULOUS MENINGITIS. HENRY H. LICHTENBERG, Am. J. Dis. Child. **43**:32 (Jan.) 1932.

In the hands of Lichtenberg, the tryptophan test appears to be of considerable differential diagnostic value in cases of meningitis in which the etiology is in doubt. This report is based on the results obtained in the examination of the spinal fluids of seventy-eight children. The test is a color reaction said to be given by the tryptophan groups when either free or combined. The positive index of a delicate violet ring at the point of contact of the fluids appeared only in those of their cases in which tuberculous meningitis was definitely demonstrated by autopsy, by inoculation of guinea-pigs or by the finding of tubercle bacilli in the fluid. The test also appears to be of positive value in the very earliest stages of tuberculous meningitis, before the physical signs of this condition are demonstrable. As a means of differentiating between encephalitis and tuberculous meningitis its value was also demonstrated. Of the seventy-eight patients studied, twenty-five were proved to be tuberculous by autopsy or by inoculation of guinea-pigs, and in all of these cases the tryptophan test was positive. When the test was negative no further signs of tuberculous meningitis developed in the patients. As a means of differentiating tuberculous meningitis from other conditions that simulate it clinically, or in spinal fluid findings, the test appears to be of great value.

LEAVITT, Philadelphia.

THE FUTURE OF MEDICINE. JOSEPH COLLINS, Psychiatric Quart. **6**:403 (July) 1932.

On the occasion of the dedication of the Medical Center at Baton Rouge, La., Collins offered several prophecies about the future of medicine. He believes that many of the scourges of the present, notably tuberculosis, cancer, the common cold and venereal disease, will have been conquered within the next century, and that the function of medicine will be largely preventive. The diseases that will bulk large in the medicine of the future will be the endocrinopathies and the neuroses. The specialist will be a glorified general practitioner, intensively trained in one field, who will devote his energies to the detection and prevention of early evidences of disease. Medicine will become progressively socialized, and the prevention and treatment of disease will be recognized as legitimate governmental functions. Collins is not impressed with the idea that this will result in a withdrawal of incentive so that the physician working for the state will become indifferent and lazy; on the contrary, he believes that under this system only men impelled by driving scientific curiosity or stimulated sincerely by the spirit of service will enter the practice of medicine. Bigotry, hatred, prejudice and self-righteousness will be properly placed in the category of disease, and the physician will combat these vices with the ardent patience that he uses to fight infections and injuries. The university medical center is considered a significant milestone in this direction.

DAVIDSON, Newark, N. J.

CREATINE AND CREATININE METABOLISM IN PROGRESSIVE MUSCULAR DYSTROPHY. M. CATHERINE MAGEE, Am. J. Dis. Child. **43**:19 (Jan.) 1932.

This study concerning the change in creatine and creatinine metabolism in muscular dystrophy is reported from observations made in two undoubted cases of dystrophy and on two control patients who were free from the disease. The author does not prove anything specifically, but she does open the way for further investigation of a larger series of cases. The observations are based on the premise that excretion of creatinine is an index of muscular development, and that the lowered excretion in muscular dystrophy may be due to the degeneration of muscle fiber, or that creatine may be formed at a slower rate than normally and, owing to the degeneration of muscle, may not be normally utilized. During the period of the observations a well balanced diet containing no meat stock was used. In these cases an inability of the body to convert creatine into creatinine and also some retardation in the formation of endogenous creatinine were demonstrated. The studies in the markedly advanced case indicated an absolute inability of the patient to convert creatine into creatinine. In the milder case excretion of creatine and creatinine remained at a lower level than is normal. Much careful work was done in the study of these cases, but except in the case of the patient with the advanced disease, definite results were wanting.

LEAVITT, Philadelphia.

A STATISTICAL STUDY OF HALLUCINATIONS IN THE MANIC-DEPRESSIVE PSYCHOSES. KARL M. BOWMAN and ALICE F. RAYMOND, Am. J. Psychiat. **11**:299 (Sept.) 1931.

Analyzing the type of hallucinations experienced in more than 1,000 patients with manic-depressive psychoses, Bowman and Raymond find that the auditory is the commonest type of hallucinatory experience. This predominance is found also in a series of schizophrenic psychoses and in a series of hallucinating patients with dementia paralytica; visual hallucinations are second and tactile experiences third in frequency, an order which is maintained not only in the cyclothymic group but also in dementia praecox and dementia paralytica. Almost three fourths of the patients in the affective class had no hallucinations, an observation that may be significantly contrasted with the datum that only 25 per cent of schizophrenic patients experienced no hallucinations. The authors call attention to the similarity

in the proportion of hallucinating patients and of the types of hallucinations among manic-depressive patients on the one hand and patients with dementia paralytica on the other. In a previous paper (*Am. J. Psychiat.* **11**:111 [July] 1931), they established the same tendency with regard to delusions in these two forms of psychoses. For all types of hallucinations and for all psychoses studied, females showed more hallucinations than males. Manic-depressive patients with seclusive personalities seemed more prone to develop hallucinations than the more extroverted types.

DAVIDSON, Newark, N. J.

HYPOPHYSEAL DYSTOSIS. J. MOREAU, Arch. franco-belges de chir. **32**:697 (Sept.) 1931.

Moreau has gathered together thirty-four cases of the Schüller-Christian syndrome and reports in detail a case observed by him. The reports collected from the literature are presented in extremely detailed abstracts, practically complete case histories. The early reports of Schüller and of Christian, together with the synthetic work of Rowland, are discussed fully, and many roentgenograms are reproduced from the original publications. The disease is characterized by four peculiarities: osteoporosis of the skull, exophthalmos, polyuria and pituitary dwarfism. The pathogenesis is probably a disturbance of the lipoid metabolism, characterized by hypercholesteremia and deposits of a xanthomatous character in the bones, particularly of the skull, and in the infundibulum, and less frequently in the skin and the internal organs.

The results of irradiation of the skull have been gratifying, and arrest of the condition or even recovery is reported. Spontaneous recovery occasionally occurs. Treatment by radiotherapy should be pursued diligently over a long period. In addition, a diet low in lipoids should be administered, and certain hypophyseal extracts are worth trying.

FREEMAN, Washington, D. C.

TUMORS OF THE HYPOPHYSEAL REGION TREATED BY RADIOTHERAPY. PARFONRY, Ann. d'ocul. **169**:651 (Aug.) 1932.

Parfonry reports three cases in which tumors of the hypophyseal region were treated with radiotherapy (in two for ten years, in the other for four years) in which improvement in the general condition, visual fields and visual acuity has been maintained throughout this period. He concludes from his observations that, although surgical treatment is important, it should be remembered that radiotherapy is of value when operation cannot be performed.

Morax reported one case in which treatment was given with radiotherapy twenty times. Visual acuity was maintained for seven years. Dupuy-Dutemps had previously reported several cases which he had followed for more than five years. In his opinion, radiotherapy should always be given a trial before operation is advised. Magitot emphasized the fact that in one of the cases presented the visual field of one eye, which had been completely abolished, was totally restored. He also stated that in certain decompressions of the chiasm Cushing had seen the visual field restored on the operating table. Sourdille reported that he preferred operation. Bollack had previously reported five cases in which the condition was favorably influenced by radiotherapy, but he believes that operation offers the best chance for recovery.

BERENS, New York.

THE MENTAL EFFECT OF THE COMPLETE MASTOID OPERATION IN CHILDREN. MACLEOD YEARSLEY, Lancet **2**:613 (Sept. 17) 1931.

On the basis of the replies to a circular letter sent to directors of a number of schools for the deaf in England, Yearsley comes to the following conclusions concerning the mental status of children in whom complete mastoidectomy has been performed: There is good evidence that complete radical operation has a markedly deterrent effect on the education of the children. In the first place, there is loss

of hearing, and in the second place, mental exhaustion and consequent inertia occur readily. The mental effect, apart from that produced by the toxemia of prolonged otorrhea, the author believes is due probably to long-continued pain together with fear of painful dressings. The condition is one of nervous exhaustion from prolonged suffering and mental strain, leading to irritability, emotional outbursts, lack of concentration, poor memory and want of balance in behavior. The effect is always more marked in children who have had to undergo more than one operation.

The accumulated data and conclusions are of interest, but it seems to the abstractor that insufficient account is taken of the defect in the eighth nerve as a psychopathologic stimulus. Furthermore, the possibility of distinct behavior defects due to fondling because of previous and prolonged serious illness is not considered.

BECK, Buffalo.

POSTENCEPHALITIC HOMOSEXUALITY. P. SCHIFF and J. O. TRELLES, Ann. méd.-psychol. (pt. 2) **89**:239 (Oct.) 1931.

One of the mental forms of epidemic encephalitis which is as yet unrecognized, according to the authors, is homosexuality, particularly in young women. A man, aged 29, with previously normal sex tendencies (?) suffered a typical oculolethargic encephalitis. For the past two years homosexual phenomena of an impulsive kind have been manifested to such an extent that, though married, he had made use of male partners. Neurologically, this patient showed a unilateral parkinsonism. In encephalitis one finds reduced sexual life and often complete frigidity. In about one third of the cases, however, there was, on the contrary, an increased sexual excitability, particularly in the chronic parkinsonism phase. Perversion, lying, stealing and violence have been shown in these stages. The question arises as to whether these are only coincidences or whether they are due to neurotropic infection. In favor of the latter explanation are the untamable impulses, the remorse and the feeling of struggle against an unconquerable force. One cannot locate a cerebral center for homosexuality, but the authors affirm that no constitutional homosexuality exists in these cases; the perversions have been set up by the encephalitis, which abolished moral self-control and the natural inhibitions. The adult is thrown back to the stage of infantile polymorphous perversity.

HART, Greenwich, Conn.

MULTIPLE GANGLIONEUROMA. HALE HAVEN and ARTHUR WEIL, Arch. Path. **13**:713 (May) 1932.

The term "ganglioneuroma" has been applied to different kinds of tumors occurring either in the central or in the peripheral nervous system in which ganglion cells have been found. Just as in the spongioblastomas one may find all transitions from the most primitive spongioblast to adult fibrillary astrocytes, so in the ganglioneuromas one may find transitions from primitive neuroblasts to adult ganglion cells. In many ganglioneuromas occurring in the brain, admixture with neoblastic glial elements may be found. A comprehensive review of this subject was given by Wahl. More recently a collection of ninety-three reports of cases from the literature was published by McFarland. They gave evidence of the various locations in the body where such tumors occur. The present case was reported because it seems to represent the only example, as far as they could determine, in which ganglioneuromas of benign type were found simultaneously in the cervical and abdominal regions, one in the region of the stellate ganglion, the others retroperitoneally. This multiple occurrence of such an adult type of ganglioneuroma has its counterpart in the multiple neuromas of Recklinghausen's disease. It is evident from the history that a neoblastic tendency was already present in the patient in early childhood.

WINKELMAN, Philadelphia.

THE TRANSIENT CHILD. MAY V. SEAGOE, J. Juvenile Research **16**:251 (July) 1932.

Frequent complaints on the part of principals and teachers that much of the disciplinary trouble in schools is due to the misbehavior of the transient children (that is, those not permanent residents of the districts) led Seagoe to study the behavior of this group in a statistical manner. She found that the comparison of data from schools between years is open to question because of the changing personnel represented by this transient class. Over 20 per cent of the children in the school districts that she studied could be classified as transients. Pupils in this group tended to be retarded in achievement, although they were generally normal in intelligence. Contrary to the popular opinion in pedagogic circles, these children did not commit more delinquencies than the permanent group; indeed, only 8 per cent of the offenses could be blamed on the temporary pupils, who constituted 22 per cent of the school census. When the offenses are grouped according to seriousness, however, a difference is marked. Of the delinquencies committed by the permanent pupils, 11 per cent were major, whereas 32 per cent of the offenses in the transient group could be so classified. It becomes apparent, therefore, that while transient pupils do not commit more delinquencies than their colleagues, they do engage in more serious ones.

DAVIDSON, Newark, N. J.

THE USE OF PENTOBARBITAL SODIUM IN PSYCHIATRY. DESMOND CURRAN and LOUIS MENSKI, Lancet **2**:223 (July 16) 1932.

Fifty-three patients with psychiatric conditions of widely different types and degree of severity were treated with pentobarbital sodium. In doses of from 3 to 6 grains (0.195 to 0.4 Gm.) it is a hypnotic of value, not unpleasant to take, certain in action, devoid of risk and free from unpleasant after-effects. It provides a sedative of definite value for cases in which there are episodic or periodic outbursts of agitation or restlessness. As a continuous sedative in prolonged cases of excitement or agitation it has value when combined with other drugs such as scopolamine. There was little evidence of increased motor restlessness after the main effect of the drug had worn off. Temporary ill effects were observed in two patients, both of whom, however, were in an extremely debilitated condition. When the drug is used in such patients the initial dose should be small, and it should be increased cautiously. No changes were observed in the urine or the central nervous system, and no significant fall in blood pressure was found except in the two patients mentioned. The drug should be given in a concentrated solution during fasting if it is to be most effective. It is doubtful whether tolerance occurs, yet there is considerable individual variation in susceptibility to the drug.

BECK, Buffalo.

BISMARSEN IN THE TREATMENT OF CONGENITAL SYPHILIS. STANLEY CHAMBERS and GEORGE KOETTER, Arch. Dermat. & Syph. **25**:1065 (June) 1932.

Bismuth arsphenamine sulphonate (bismarsen) is considered the remedy of choice in the treatment of children with syphilis. When given intramuscularly, it is more readily administered than when used intravenously. The dosage varies from 10 mg. for a new-born infant to 75 mg. for a child of 3 months, 100 mg. for a child of 1 year, and 200 mg. for children more than 5 years of age. The injection is given into the buttock, in an area not recently used for a previous injection. Confinement to any one quadrant of the nates is not necessary. After the injection the area is massaged deeply with a heavy, pestle-like instrument. The dose is given twice a week. If the bismarsen is filtered through gauze, no untoward local reaction should occur. The authors gave 6,400 injections without producing any toxic effects. The Wassermann reaction was made negative in 81 per cent of the patients who received biweekly inoculations and in 65 per cent of the group who received injections only once a week. The spinal fluid showed no change under this treatment. Most of the manifestations of congenital syphilis show marked improvement, the clearing of interstitial keratitis being especially gratifying.

DAVIDSON, Newark, N. J.

HALLUCINATIONS AND MENINGIOMAS OF THE LITTLE WING OF THE SPHENOID. M. DAVID and P. PUECH, Encéphale **27**:409 (May) 1932.

With the inclusion of two cases of meningiomas in the region of the lesser wing of the sphenoid, the authors come to the conclusion that such tumors give rise to a syndrome analogous to that of a temporal glioma. All forms of hallucinations described for the latter can be found in the sphenoidal meningioma group. One case was characterized by a "dreamy state," the other by olfactory hallucinations. In others reported in the literature, visual and gustatory hallucinations have been observed. However, in any given case the hallucinations seem always to be of the same kind; diverse forms are not as frequent as in glioma. This hallucinatory syndrome is comparatively rare, being found in only 8 per cent of twenty-five verified cases of meningioma of the sphenoid. On the other hand, Cushing showed that 40 per cent of forty-five cases of temporal glioma were accompanied by uniform crises. In all tabulated cases the hallucinatory phenomena have been early manifestations and thus assume some diagnostic importance.

ANDERSON, Los Angeles.

THE ANTISYPHILITIC ACTION OF THE MALARIAL PARASITE IN OTHER THAN CENTRAL NERVOUS SYSTEM SYPHILIS. CHARLES C. DENNIE, HARRY M. GILKEY and SIDNEY F. PAKULA, Am. J. Syph. **15**:320 (July) 1931.

Malaria, the authors believe, has a general antisyphilitic action and is effective for visceral syphilis as well as for dementia paralytica and tabes. They take issue with the hypothesis that the effectiveness of malarial therapy depends on the heat produced, preferring Breutsch's theory that macrophages cast off from vascular endothelia destroy the spirochetes by using them as food. They condemn the attempt to produce fever by other means (such as diathermy or foreign protein) as unsound. They studied five children and an adult with visceral syphilis, who were inoculated with malaria; two of the children had neither chills nor fever, although even these two yielded positive blood smears. The other patients had from three to ten chills. Excellent results were obtained in keratitis, bone syphilis and joint involvements. They also believe that after a course of malaria the patient's response to antisyphilitic therapy of other forms is improved.

DAVIDSON, Newark, N. J.

PARKINSON'S SYNDROME IN RELATION TO TRAUMATISM. J. V. COLARES, An. assist. a psicop., 1931, p. 141.

Colares recalls that the question as to whether Parkinson's syndrome may be of traumatic origin has been, for many years, a matter of controversy. A short time ago, the author had an opportunity to observe in the Pinel section of the Hospital Nacional, a case of Parkinson's syndrome apparently of traumatic origin, which led him to study in the neurologic literature the question of the relation of traumatism to Parkinson's syndrome. The case was a typical one, and the patient stated that he had enjoyed perfect health up to the time that he suffered a severe trauma, a short time after which the symptoms of Parkinson's syndrome began to appear. A careful examination of the patient's personal history and of the patient himself excluded at first the intervention of any etiologic factor other than traumatism. At the cost of much time and patience, however, the author was able to reconstruct with great minuteness the history of the case, so that there appeared from the personal history, as was later proved, certain factors pointing to the causal influence of epidemic encephalitis. The complete personal history of the patient is given.

EDITOR'S ABSTRACT.

THE BASIC SYMPTOMS OF SCHIZOPHRENIA. MAX LEVIN, Am. J. Psychiat. **11**:215 (Sept.) 1931.

The basis of schizophrenia is the characteristic alteration in thinking, in feeling and in relations with the outer world; the delusions and hallucinations are secondary symptoms of only accessory importance. Recognition of the basic alterations in content and trend of thought is necessary in the successful management of incipient dementia praecox. Ambulatory patients usually experience no hallucinations, yet present well marked basic symptoms. By way of illustration, Levin cites fourteen cases of early schizophrenia, in none of which were there frank hallucinatory episodes, but in all of which there were the disorders in association and ideation characteristic of schizophrenic thinking. Misinterpretations of words, round-about oddities of logic, significant puns and instances of apparent want of emotional expression are cited as illustrative of the basic symptoms of dementia praecox. The examples are well chosen, and the presentation owes its clearness to the concreteness of the illustrations; for this reason, the paper should be read in full.

DAVIDSON, Newark, N. J.

SCIATICA AS AN EARLY SYMPTOM OF PULMONARY TUBERCULOSIS. L. S. MINOR, Mod. neuropsychiat. (Kharkov) **7**:73, 1931.

The pain from pathologic conditions of various internal organs is often radiated to distant areas of the body. The various radiation zones of referred pains were mapped out by Head in his monumental work. The sudden development of sciatica in a young person may often be associated with disease of some viscus. In 1883, Landouzy, in a paper in *Gazette des hôpitaux* entitled "Sciatique prétuberculeuse pulmonaire," pointed out the connection between sciatica and incipient tuberculosis. Since 1880, Minor has paid special attention to the combination of these two conditions and has collected a large series of cases. He illustrates his point with reports of fifteen cases, and discusses various clinical points. He emphasizes that, while in atypical sciatica the achilles reflex is lost, it is commonly present in the syndrome he describes; often it is increased. A thorough physical examination, especially of the lungs, is urged, as a serious pulmonary outbreak may be prevented.

KASANIN, Boston.

HISTOLOGIC STUDIES OF THE BRAIN IN CASES OF FATAL INJURY TO THE HEAD. CARL W. RAND, Arch. Surg. **22**:738 (May) 1931.

Following severe injury to the head there is a generally distributed increase in the quantity of fluid in the skull; the brain is heavier than normal, and the spinal pressure is increased. To determine the source and physiology of this excess fluid, Rand studied the brains of sixty-one persons who had died following an injury to the head. He reviews the evidence pointing toward a secretory function of the choroid plexus; in his study, he found distention of the choroidal epithelia, enlargement of the associated blood vessels and granular pigmentation. In normal brains, vacuolation of the choroidal epithelia was found in 15 per cent of the cells; following trauma, vacuoles were found in more than half the cells. Somewhat similar changes occurred in the ependymal cells. This contribution is a preliminary report, subsequent papers being promised to consider these changes in greater detail.

DAVIDSON, Newark, N. J.

SUICIDE IN THE ARMY. P. SCOURAS, Hyg. ment. **26**:153 (July-Aug.) 1931.

This study is replete with case histories. In summary, some attempt at a rough classification is made. The first group comprises men in whom the attempt at suicide is a mode of reaction related to a mental equipment insufficient for the trials of military life. The second group is composed of subjects unadaptable to military life—refractory to discipline and the like. In a general way this group might be placed in the so-called "psychopathic" category. The third group includes alcoholic and encephalitic persons; these are pathologic per se, and

military life has little influence on them. The fourth group contains the patients suffering from anxiety and obsessional neuroses—reactions to an internal compulsion which may, in predisposed persons, be favored in the military milieu. The fifth group includes persons subject to simulation or malingering, who present, of course, diverse etiologies at the base. A preexisting disequilibrium is almost to be assumed.

ANDERSON, Los Angeles.

VISCEROCARDIAC REFLEXES. H. G. SCOTT and A. C. IVY, Arch. Int. Med. **49**:227 (Feb.) 1932.

To study the mechanisms of viscerocardiac reflexes, Scott and Ivy experimented on frogs and dogs. In the decerebrate frog, allowing time for shock to pass and avoiding anesthesia during stimulation, they opened the abdomen and stimulated the gallbladder. Incision of the gallbladder caused a marked reduction in heart rate; excision of the intact gallbladder left the heart rate unaffected, provided there was no spilling. If bile was spilled into the upper peritoneal cavity, cardiac inhibition occurred. This was not due to the irritation of the bile on the heart itself, since pouring bile over the pericardium caused no inhibition. Pinching the abdominal and pelvic viscera did cause cardiac inhibition, although simple pinching or pulling of the gallbladder without tearing was usually ineffective. Greater effects were produced when the bile was darker. Similar experiments were performed on dogs, but the results were less definite. From this work, it appears that there is a viscerocardiac reflex mechanism, the sensory neuron of which begins in the upper part of the peritoneum.

DAVIDSON, Newark, N. J.

CEREBRAL ANEURYSM WITH RECURRENT LEAKAGE. R. M. J. HARPER, Brit. M. J. **1**:13 (Jan. 2) 1932.

The author reports the case of a woman, aged 41, who had been in perfect health until about one and a half years before, when she began to complain of premenstrual headaches. On March 7, 1931, she was in the premenstrual period. She complained of severe headaches, and later in the day she fell and became unconscious. Aphasia remained after consciousness was regained. She steadily improved until April 4, when she again became unconscious, this time with evidence of more extensive cerebral damage. A spinal fluid tap revealed blood in the fluid and on standing a yellow color. A diagnosis of leaking aneurysm in the location of the left sylvian fissure was made. On April 10, the patient died of bronchopneumonia. Necropsy revealed a small aneurysm, probably congenital, surrounded by clot at the origin of one of the branches of the left middle cerebral artery. A very small opening in the aneurysm revealed the source of leakage.

FERGUSON, Niagara Falls, N. Y.

THE EFFECT OF VARIOUS FACTORS ON EXPERIMENTALLY PRODUCED CONVULSIONS. HADDOW M. KEITH, Am. J. Dis. Child. **41**:532 (March) 1931.

To produce convulsions, Keith used thujone, the chief constituent of oil of absinth. He selected wormwood because this drug affects particularly the intact cortex. A 1 per cent solution suspended in gum acacia was used intravenously. It was determined that 0.35 cc. of this solution per kilogram of body weight was a normal convulsing dose, and this was taken as a standard. When rabbits were dehydrated with sucrose, standard convulsing doses of thujone failed to produce convulsions; this same protection, however, was not afforded by drastic dehydration by complete restriction of fluid for a period of four days. Acetone and diacetic acid were injected intravenously and thujone was then introduced and found less effective than on rabbits that had not received acetone bodies. These acetone preparations did not cause dehydration of the cerebral tissue.

DAVIDSON, Newark, N. J.

RELATION OF THE INCIDENCE OF EPILEPTIC SEIZURES TO COSMIC AND GEOPHYSICAL PHENOMENA. ALPHONSO FRESA, Arch. gen. di neurol., psichiat. e psicoanal. **13**:21 (April 30) 1932.

An epileptic patient, aged 30, well educated and of superior mentality, a teacher by profession, had had seizures since the age of 12, at first monthly, then bimonthly, and for the latter years trimonthly. Since 1926, he had kept a careful and detailed account of all the seizures and "equivalents." Fresa compares this "calendar" of the patient's attacks with the lunar phases, with the manifestations of solar activities (solar spots, etc.) and with various geophysical phenomena. From this study he concludes that there exist relations between the incidence of epileptic attacks and cosmic and geophysical phenomena. The incidence of complete epileptic fits seems to be influenced by the lunar phases, whereas the incidence of the "equivalents" appears to be favored by phenomena of solar activity.

YAKOVLEV, Palmer, Mass.

ETIOLOGY OF THE SYNDROME OF THE NASAL NERVE. C. CHARLIN, Ann. d'ocul. **169**:257 (April) 1932.

The syndrome of the nasal nerve has been discussed by Charlin in two previous communications (*Ann. d'ocul.* **168**:86 [Feb.]; 808 [Oct.] 1931). In this paper he considers the etiology of the syndrome of the nasal nerve and points out that in the presence of the triad he has discussed, that is, inflammation of the anterior segment of the eye, coryza with profuse watery nasal discharge and oculo-orbital neuralgia, examination should not be limited to exploration of the nasal cavity. He reports a case of the syndrome of the nasal nerve relieved of symptoms by the removal of several infected teeth. In the treatment of these conditions he first suggests applications of medicaments in the nose. If this does not relieve the condition in a few days a more general cause should be sought. If a nasal pathologic condition or nasal deformities are found, these should be corrected.

BERENS, New York.

PUBLIC HEALTH SERVICE AND MENTAL HYGIENE IN THE U. S. S. R. L. ROSENSTEIN, Ment. Hyg. **15**:739 (Oct.) 1931.

In Soviet Russia the state medical department is a public institution for the prevention and treatment of disease, much like the community fire department. Stress is laid on the prevention of mental disease and the protection of the mother, the child and the adolescent. Large programs of psychologic research have been undertaken with the enormous material placed at the disposal of the department through industrial and dispensary connections. "Pedology" has been created as a science to study the psychophysical development of the child from birth to maturity, and guidance clinics abound throughout the country. All criminals receive psychiatric study, and scientific methods, Rosenstein says, are proving a potent form of social therapy. There are no juvenile courts, young delinquents being studied by commissions consisting of educators, sociologists and psychiatrists, and not by lawyers and judges.

DAVIDSON, Newark, N. J.

TORSION-SPASM (DYSTONIA LENTICULARIS). HUGH G. GARLAND, J. Neurol. & Psychopath. **12**:193 (Jan.) 1932.

A Jewish boy, aged 17, had become ill in the spring of 1918, at the age of 5, with malaise, tremor and weakness of the right hand, dysarthria and difficulty in standing. His condition improved in the next two years, but thereafter became worse, with weakness of hemiplegic distribution, severe involuntary spasms, marked kyphoscoliosis, wasting of the right arm and leg, cogwheel rigidity, spasmodic breathing and slight pupillary irregularity with nystagmoid jerks. A Babinski sign had appeared recently, without reflex changes. The patient had been operated

on for contracture of the tendo achillis. There were no sphincteric, sensory or intellectual disturbances. The author believes that this is a case of torsion spasm, with involvement of the pyramidal system, but he could not exclude a possible post-encephalitic manifestation.

SPERLING, Philadelphia.

MENINGITIS DUE TO BACILLUS ACIDI-LACTICI IN A NEW-BORN INFANT. HARRY D. PASACHOFF, Am. J. Dis. Child. **41**:862 (April) 1931.

To the three cases of meningitis due to the lactic acid bacillus already reported, Pasachoff adds a fourth. His patient was 10 days old when a slight fever developed; convulsions occurred on the following day and continued. The child became weaker and died thirteen days after the onset of the symptoms. There was no Kernig sign, stiffness of the neck or retraction of the head. There was a dry exudate at the site of a circumcision. Three spinal taps were done, and on each a pure culture of a nonmotile form of Bacillus acidi-lactici was obtained. Pasachoff reviews the possible modes of entry, considering intra-uterine infection, intra-uterine aspiration of amniotic fluid and an infection through the circumcision wound. The lactic acid bacillus is ordinarily without pathogenic significance.

DAVIDSON, Newark, N. J.

DIAGNOSIS OF DISSEMINATED SCLEROSIS BY GRAPHIC REGISTRATION AND FILM TRACKS. F. JANVIN and C. WORSTER-DROUGHT, Lancet **2**:1384 (Dec. 24) 1932.

On the basis of the examinations in a large group of cases, it is assumed by Janvin and Worster-Drought that all cases of disseminated sclerosis, apart from those with a purely spinal localization, will reveal themselves by the presence of waves of ataxia in graphic registration. The tests were accomplished by two methods: by a modified kymograph, in which the diaphragm is placed over the mouth, or by means of a sound track film. Although the majority of cases studied were mild, with no alteration of the voice to be detected by ear even with the most attentive listening, this was always an "ataxic" defect. The test is therefore ultra-acoustic. All diseases or lesions producing laryngeal ataxia, however, register in the same way. Graphic records of speech in disseminated sclerosis had been made in 1916.

BECK, Buffalo.

BODY STRUCTURE IN DEMENTIA PARALYTICA. J. BITTENCOURT, An. assist. a psicop., 1931, p. 207.

Bittencourt describes in detail the body structure of fifty patients with dementia paralytica (forty-six men and four women). He found it more difficult to isolate structural types in members of the female sex, hence, in order to avoid greater sources of error, he included only four women. The patients selected were all over 30 years of age. The author concludes from his extensive research: There is no neuro-endocrine formula of body structure, but a combination of facts shows that body structure is a "function" of the neuro-endocrine system. In the fifty patients with dementia paralytica, the pyknic (thick-set) type of body structure predominated, which confirms the observations and impressions of other authors. The predominance over the other types was not very great, but is more significant when one recalls that among normal persons the pyknic type is the least frequent.

EDITOR'S ABSTRACT.

PREPARATION OF EXTRACTS OF THE ANTERIOR PITUITARY-LIKE SUBSTANCE OF URINE OF PREGNANCY. P. A. KATZMAN and E. A. DOISY, J. Biol. Chem. **98**:739 (Nov.) 1932.

The authors review previously used methods for the preparation of purified extracts from hypophyses or urine of pregnant women. They give the details of

preparation by two new methods. One depends on the absorption of the active principle by norit and elution with phenol. The other, recommended as more rapid and simple, depends on its absorption on finely divided benzoic acid and elution by dissolving the benzoic acid in acetone. By this means extracts having a potency of 1,250 mouse units per milligram have been obtained, increased to over 3,000 units by fractional precipitation with acetone. The immature mouse and rat units based on opening of the vagina and estrus are defined.

DAILEY, Boston.

CHRONIC ENDEMIC ERGOTISM: ITS RELATION TO THE VASOMOTOR AND TROPHIC DISEASES. JULIUS KAUNITZ, Arch. Int. Med. **47**:548 (April) 1931.

Many cases of Buerger's, Raynaud's and similar vasomotor diseases are due, Kaunitz is convinced, to chronic ergotism. He quotes a bulletin of the Department of Agriculture which reports heavy ergotization of American rye. He reviews the symptomatology of various peripheral vascular diseases, and compares them clinically and pathologically to the gangrene produced experimentally by feeding ergot to chickens. He takes issue with the opinion of Buerger that except in thrombo-angiitis obliterans, the pathologic effects of the peripheral vascular diseases are a result of neurotrophic disturbances, pointing out that other conditions, such as endarteritis, are usually present. He concludes with a plea for the more careful protection of rye from the mycelium of ergot. The paper is illustrated with instructive photomicrographs.

DAVIDSON, Newark, N. J.

TREATMENT OF EPILEPSY. W. GRÜNDLER, Psychiat.-neurol. Wchnschr. **33**:157 (April 4) 1931.

A combination of bromine with phenobarbital, in which the former is alleged to act on the cerebral cortex and the latter on the brain stem, was used in the treatment of epilepsy. The authors used institutional epileptic patients in their experiments. There was some diminution in seizures, but this was not observed with the use of the former smaller doses. No particularly favorable influence in the cases of petit mal was reported. A specific effect on epilepsy was observed to come more rapidly after phenobarbital than after the combination. Because of the supposed sphere of action of the two drugs the effect of the phenobarbital seems to be the more important, whereas the amount of phenobarbital in the combination was too slight to be effective.

HART, Greenwich, Conn.

THE INFLUENCE OF STIMULATION OF THE SYMPATHETIC ON THE EXCITABILITY OF THE SENSORY FIBERS OF THE SCIATIC NERVE IN CATS. R. TSUJI, Arch. f. d. ges. Physiol. **228**:434, 1931.

The chronaxia of the centripetal fibers of the sciatic nerve was measured in decerebrated cats; at the same time a record of the ipsilateral quadriceps muscle was made. The stimulation of the lumbar part of the sympathetic chain produced in eight cats a shortening, in three a lengthening and in two no changes of the chronaxia. The tetanic contraction of the muscle was increased in nine cats, lowered in two and unchanged in one by the stimulation of the sympathetic. The author concludes that the sympathetic shortens the chronaxia and increases the excitability; the opposite effect observed in some of his experiments is explained by the excitation of hypothetic parasympathetic fibers in the sciatic nerve.

SPIEGEL, Philadelphia.

NEW METHOD FOR DIAGNOSIS OF NEUROSYPHILIS. A. CERQUEIRA LUZ, An. assist. a psicop., 1931, p. 165.

Luz uses for the examination of cells a postvital staining method, employing Pappenheim's solution (methyl green; pyronin), and a fixation method, employing Pappenheim's method (May-Grünewald-Giemsa stain). His positive results were in close accord with the anatomopathologic observations, which reveal in the nerve

centers of neurosyphilitic patients an extensive lymphoplasmatic infiltration, which in the cases showing a remission is modified, the plasma cells being no longer found, while there is a diminution of the lymphocytes. In the negative cases (absence of neurosyphilis), in addition to an abundant increase of cells, amounting to from 3,000 to 4,000 per cubic millimeter, he found always a neutrophil polymorphonucleosis.

EDITOR'S ABSTRACT.

THE SIGNIFICANCE AND VALUE OF THE LANGE GOLD SOL REACTION IN DISSEMINATED SCLEROSIS. HELEN J. ROGERS, J. Neurol. & Psychopath. **12**:205 (Jan.) 1932.

The author reviews the literature and reports her own findings in the spinal fluid in seventy cases of multiple sclerosis, her results and those of previous writers being in essential agreement. It was found that "25 per cent show completely normal Lange colloidal gold sol curves; 25 per cent show paretic curves, and 50 per cent show almost every possible intermediary curve between the normal and paretic zone." No definite parallelism exists between the clinical course and the changes in the spinal fluid. The fluid was found to alter both spontaneously and following treatment of all kinds, with and without a corresponding clinical modification. The Lange colloidal gold reaction cannot therefore be used as a therapeutic criterion, nor does it have any real value in disseminated sclerosis.

SPERLING, Philadelphia.

SPONTANEOUS SUBARACHNOID HEMORRHAGE. ARTHUR J. HALL, Lancet **1**:222 (May 28) 1932.

Seven cases of subarachnoid hemorrhage are presented, in six of which the patients recovered. The well known symptomatology of subarachnoid hemorrhage is reviewed. Three of the author's cases showed exacerbations of symptoms, two apparently without additional bleeding, and one with recurrent bleeding even more severe than the initial attack. One patient had a severe epileptic seizure eleven days after such an exacerbation; it is suggested that it might have been due to absorption of blood. Another patient, a woman, aged 46, recovered from an attack almost identical with one that her mother had had at the age of 62. The question of therapeutic lumbar puncture is discussed. Its value other than to relieve intracranial pressure is questionable.

BECK, Buffalo.

ELECTROBIOLOGIC SYMPTOMS ON THE CORTEX CEREBRI. M. H. FISCHER, Arch. f. d. ges. Physiol. **230**:161, 1932.

The electrical currents of the cortex were studied in rabbits, cats, dogs and monkeys. Spontaneous changes of the potentials are at least partly due to states of excitation of the cortex. Such spontaneous changes appear sometimes in "fits." Toxins like strychnine and morphine facilitate their appearance. Stimulation of an eye by light produces action currents of the contralateral area striata. The currents appear at the beginning and at the end of the stimulation and are of rhythmic type. The potential difference is from 1 to 2 millivolts. The action currents are a sign of cortical activity; they are missed if the electrodes are placed on the white substance.

SPIEGEL, Philadelphia.

LYSOZYME IN SALIVA. NICHOLAS KOPELOFF, MEYER M. HARRIS and BARBARA MCGINN, Am. J. M. Sc. **184**:632 (Nov.) 1932.

An attempt was made to corroborate the work of Penrose, who found the lysozyme content of saliva in dementia paralytica and in postencephalitic parkinsonism to be diminished. With well controlled and accurate standards no differences could be discerned between the lysozyme content of the saliva of fourteen patients with postencephalitis and fourteen normal persons. It was thought that Micrococcus lysodeikticus was a stable culture and could be used as a measure of the lytic principle present in human secretions.

MICHAELS, Boston.

CEREBELLAR ABSCESS. SYDNEY NUSSBAUM AND GEORGE WEBB, Am. J. Dis. Child. **43**:147 (Jan.) 1932.

The authors' case of suspected brain abscess in a child of 11 years demonstrates the wisdom of watchful waiting until localization in the infected area takes place, before operative procedures are attempted. The case developed from otitis media on the left side; signs indicative of inflammation of the left lobe of the cerebellum gradually appeared, and later those of increased intracranial pressure. The interesting feature of the case is that the patient recovered without any apparent residual signs of damage to the central nervous system.

LEAVITT, Philadelphia.

THE DIRECT STIMULATION OF THE RED NUCLEUS IN CATS. W. R. INGRAM, S. W. RANSON and F. I. HANNETT, J. Neurol. & Psychopath. **12**:219 (Jan.) 1932.

From experiments on twenty-one cats with intact brains, in which they used the Horsley-Clarke stereotaxic instrument and a weak faradic current to focalize the stimulus, the authors conclude that the red nucleus is not the site of origin of the typical segmental response. This response consists of curving of the back and neck, with concavity toward the stimulated side, associated with flexion of the ipsolateral forelimb, and often extension of the contralateral forelimb. The focal point for this reaction is the reticular formation of the tegmentum of the mesencephalon and pons.

SPERLING, Philadelphia.

INFLUENCE OF THE EYE ON THE GROWTH OF ITS ASSOCIATED STRUCTURES, STUDIED BY MEANS OF HETEROPLASTIC TRANSPLANTATION. VICTOR C. TWITTY, J. Exper. Zool. **61**:333 (April 5) 1932.

Single eyes were interchanged between larvae of Amblystoma punctatum and of A. tigrinum by embryonic heterotransplantation. The eye exerts an important influence on the growth of its related extrinsic structures. The sclerotic capsule, ocular muscles and optic brain centers partially adjust their proportions to the scale indicated by the size of the transplanted organs. The results are regarded as instances of true correlative growth, in which the growing eye exerts a dynamic influence on the developing extrinsic ocular structures.

WYMAN, Boston.

PARASYMPATHETIC INFLUENCE ON THE NEUROMUSCULAR APPARATUS. H. ALTENBURGER and F. W. KROLL, Arch. f. d. ges. Physiol. **230**:349, 1932.

The posterior roots of the lumbar and sacral segments were severed in cats, and their distal end was stimulated. The chronaxia of the musculus gastrocnemius was shortened by this stimulation in normal animals; it was lengthened in decerebrated animals. Extirpation of the sympathetic chain also reversed the effect of the stimulation of the posterior roots on the muscular chronaxia. The authors assume that their experiments show the existence of a parasympathetic innervation of the skeletal muscles through centrifugal impulses in the posterior roots.

SPIEGEL, Philadelphia.

ARCHITECTONIC LOCALIZATION BASED ON BIO-ELECTRIC MANIFESTATIONS IN THE CEREBRAL CORTEX. I. A CONTRIBUTION TO THE STUDY OF THE PUPILLARY REACTION TO LIGHT IN THE GUINEA-PIG. A. E. KORNMÜLLER, Jahrb. f. Psychol. u. Neurol. **44**:447, 1932.

Illumination of the eyes of guinea-pigs was followed by bio-electric manifestations on the exposed cortex. These phenomena could be definitely localized in definite architectonic areas of the area striata and peristriata. These architectonic areas apparently have also bio-electric characteristics on the basis of which these areas may be clearly outlined in the living brain.

KESCHNER, New York.

CEREBRO-SPINAL FLUID PRESSURE IN SYPHILIS. T. F. HEIVER, Lancet **1**:222 (May 14) 1932.

In a series of 313 cases of syphilis, routine examinations were made of the spinal fluid. Increased pressure was the least common abnormality, and there was no apparent relationship between the degree of pathologic change and the pressure of the fluid. Therefore, there appears to be little evidence that increased pressure of the cerebrospinal fluid is either a common or a reliable indication of syphilis of the nervous system, and the constant quotation of this sign in textbooks is the result of inaccurate observation.

BECK, Buffalo.

TRAUMATIC ENOPHTHALMOS AND FRACTURE OF THE ORBIT. M. DE TREIGNY, GIRARD and BOULAN, Ann. d'ocul. **169**:316 (April) 1932.

De Treigny, Girard and Boulan report the case of a child, aged 2½ years, who, eight months previous to examination, had been in a severe automobile accident. The skull had been injured in the occipital region. The eyeball showed marked enophthalmos, but motility was normal. The iris reacted poorly to direct light. The orbit and the cranial cavities were apparently in communication because the eye pulsated synchronously with the pulse.

BERENS, New York.

HISTOPATHOLOGY OF TRAUMATIC NEUROMAS. B. A. FAWORSKY, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:399, 1932.

The architectonic formation of traumatic neuromas begins with changes in certain nerve bundles, the others being normal. The neuromatous formation may begin in a circumscribed area in the peripheral part of the nerve stump; it may occur simultaneously in several areas, or it may be limited to the central portion of the nerve. Mechanical factors determine the various modes of formation of the neuromas. In 85 per cent of the cases there are inflammatory reactions in the tumors.

ALPERS, Philadelphia.

A CASE OF INTERMITTENT EXOPHTHALMOS. E. DELORD and H. VIALLEFONT, Ann. d'ocul. **169**:730 (Sept.) 1932.

A case of intermittent exophthalmos is reported by Delord and Viallefont. The attacks occurred during a period of eight months, the protrusion of the eyeball being more frequent and the duration of the attacks longer in the later months of the disease. The blood pressure in the retinal arteries was elevated to 150 mm. of mercury during one attack. Prolonged compression of the carotid for a month resulted in complete cure. The authors believe that the exophthalmos was due to an arteriovenous aneurysm of the carotid.

BERENS, New York.

NEUROLOGIC SYNDROMES ASSOCIATED WITH HYPOGLYCEMIA. ARCHIE D. CARR, J. A. M. A. **97**:1850 (Dec. 19) 1931.

Neurologic symptoms associated with moderate hypoglycemia are weakness, restlessness, sweating, anxiety and hunger. In more advanced hypoglycemia there is a varying degree of stupor, sometimes with convulsions and loss of reflexes. Hemiparesis has been reported. Many patients recover, according to Cannon, McIver and Bliss, because hypoglycemia activates the splanchnic neurons of the sympathetic system, as indicated by an increased secretion of epinephrine which restores equilibrium.

JENKINS, Indianapolis.

BLUE STAIN OF THE SCLERA (FALSE BLUE SCLERA). H. VIALLEFONT, Rev. d'oto-neuro-opht. **10**:696 (Nov.) 1932.

A patient presented blue coloration of the sclera of both eyes, which was limited to an irregular ring, 6 mm. in diameter, near the limbus. The skin of the

lids was also blue. Vision was good, and no other areas of pigmentation were found. No stigmas of van der Hoeve's syndrome were observed. The patient was syphilitic. The pigmentation was a local accident and was not part of the syndrome of van der Hoeve.

DENNIS, Colorado Springs, Colo.

THE INFLUENCE OF STIMULATION OF THE SYMPATHETIC AND THE PARASYMPATHETIC ON THE CONTRACTIONS OF THE CAT'S TONGUE. E. SCHILF and W. F. STERNBERG, Arch. f. d. ges. Physiol. **229**:758, 1932.

Contractions of the cat's tongue were produced by rhythmic stimulation of the nervus hypoglossus. During this stimulation the cervical sympathetic was stimulated and the height of the contractions was consequently lowered. This effect was not observed if the carotid artery was clamped. Stimulation of the vasodilator fibers of the chorda tympani had no effect.

SPIEGEL, Philadelphia.

EVOLUTION OF IDEAS ON HALLUCINATIONS. HENRI CLAUDE and HENRI EY, Encéphale **27**:361 (May) 1932.

This article is a long discussion of the history and evolution of the ideas as to what constitutes hallucination. It starts with the original formulation of Esquirol, in 1817, that an hallucination is an internal conviction of a sensation without any external stimulus object. After tracing through the complex psychologic formulations of the intervening years, the conclusion is reached that that early formulation is still essential and sound.

ANDERSON, Los Angeles.

A CASE OF ARACHNOIDITIS INVOLVING THE CHIASM AND OPTIC NERVES. BRETAGNE and MICHON, Ann. d'ocul. **169**:232 (March) 1932.

A patient, aged 20, suffered rapid diminution of vision for one month without ophthalmoscopic signs. At the end of a month, papilledema was noted in both eyes, associated with a large central scotoma. At the end of three months the disks were atrophic and pale. The skull was opened by the transfrontal route, and a diagnosis was made of arachnoiditis of the optic chiasm and optic nerves, with increased intracranial pressure due to mild internal hydrocephalus.

BERENS, New York.

POLYNEURITIS FROM TRICRESYL PHOSPHATE. BENJAMIN T. BURLEY, J. A. M. A. **98**:298 (Jan. 23) 1932.

The typical symptoms of neuritis caused by tricresyl phosphate are motor paralysis with reaction of degeneration in the paralyzed muscles and absence of sensory and cranial nerve changes. The poison effects the peripheral nerve changes. The pathologic process is focal degeneration of the myelin sheath and axis cylinder, especially of the anterior tibial, external popliteal and ulnar nerves. Sections of the spinal cord show indefinite changes in the anterior horn cells.

JENKINS, Indianapolis.

CEREBRAL ADIPOSITY WITH NERVE DEAFNESS, MENTAL DEFICIENCY AND GENITAL DYSTROPHY: A VARIANT OF THE LAURENCE-BIEDL SYNDROME. EDWARD WEISS, Am. J. M. Sc. **183**:268 (Feb.) 1932.

Two cases in one family are reported in which deafness took the place of retinitis pigmentosa as a mutual equivalent. This cannot be explained as a genetic defect of the forebrain because of the known origin of the auditory nerve from the hindbrain. A conservative attitude that further embryologic investigations may shed light is expressed.

MICHAELS, Boston.

AN EPIDEMIC OF CHOREA IN A FAMILY. DONALD PATTERSON and LOUIS J. HORN, Brit. M. J. **2**:893 (Nov. 14) 1931.

Three cases of chorea are reported as occurring almost simultaneously in one family. The entire family slept in one rather small, poorly ventilated room. The father was said at the time to be suffering from rheumatic arthritis, though there was little swelling of the joint. The fourth child in the family had chronically infected tonsils; the authors think that he was probably the source of infection for the afflicted children.

FERGUSON, Niagara Falls, N. Y.

THE "CONDITIONED REFLEX" IN RELATION TO FUNCTIONAL DISORDERS IN CHILDREN. MAX SEHAM, Am. J. Dis. Child. **43**:163 (Jan.) 1932.

This study of reflex activity is essentially a résumé and criticism of the existing literature on this subject, beginning with the studies of Descartes and discussing those of Sechenov, Sherrington, Thorndike, Pavlov and Krasnogorski. No new or original observations are proffered by the author, and he quotes copiously from the works of the physiologists mentioned. The bibliography is particularly complete and is of value to students of "behaviorism."

LEAVITT, Philadelphia.

HAEMANGIOMA OF VERTEBRA: A CAUSE OF COMPRESSION OF THE CORD. F. J. NATTRASS and DONALD RAMAGE, J. Neurol. & Psychopath. **12**:231 (Jan.) 1932.

In a man, aged 51, with signs of compression of the cord from a hemangioma of the thoracic vertebra, excellent clinical improvement was obtained by high voltage roentgen treatment. Only two similar cases with recovery have been reported in the literature, both in patients who received roentgen therapy following operation. The authors suggest that roentgen therapy is indicated primarily.

SPERLING, Philadelphia.

SPASM OF THE CENTRAL ARTERY OF THE RETINA AFTER ACUTE POISONING BY GARDENAL. J. DUBAR, P. MASQUIN and DUBLINEAU, Ann. d'ocul. **169**:141 (Feb.) 1932.

Dubar, Masquin and Dublineau report the case of a man, aged 27, who attempted suicide by taking 2 Gm. of a brand of phenobarbital (Gardenal). After a period of somnolence, bilateral spasm of the central arteries occurred. Visual acuity returned to normal following two injections of acetylcholine.

BERENS, New York.

THE INTRAVENOUS LIVER TREATMENT OF PERNICIOUS ANAEMIA. I. BILLIG, W. N. WEST-WATSON and C. J. YOUNG, Brit. M. J. **1**:273 (Feb. 13) 1932.

The authors report their results in the treatment of two patients with pernicious anemia by means of the intravenous administration of liver extract. Both responded rapidly, although one had previously failed to respond to the oral administration of liver owing to vomiting, and the condition of the other was complicated by sepsis.

FERGUSON, Niagara Falls, N. Y.

A CASE OF RETINITIS PIGMENTOSA WITH POLYDACTYLISM. BAILLIART and SCHIFF-WERTHEIMER, Ann. d'ocul. **169**:314 (April) 1932.

A girl, aged 14, who had six digits on each hand, had presented no sign of retinitis pigmentosa until she was 12 years of age, after a severe typhoid affection, when typical retinitis pigmentosa was discovered. The patient suffered from hereditary syphilis, but was the only one in her family who had polydactylism and a disease of the eyes.

BERENS, New York.

PATHOGENESIS OF DIABETES INSIPIDUS. V. N. RUSSKIKH and E. S. KRILOVA, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:412, 1932.

In a case of diabetes insipidus of long duration there were degenerative changes in all cells of the tuber cinereum except the corpora mamillaria. Furthermore, the hypophysis was small, the posterior lobe was sclerosed and the anterior lobe was atrophied.

ALPERS, Philadelphia.

TREATMENT OF NARCOLEPSY WITH EPHEDRINE. HENRY COHEN, Lancet **2**:335 (Aug. 13) 1932.

Nine patients whose condition was diagnosed as narcolepsy were treated. The results obtained were similar to those recorded before by Doyle and Daniels. All patients improved, the majority benefiting considerably from ephedrine therapy.

BECK, Buffalo.

HEREDITY AND EPILEPSY. J. S. MASON, Brit. M. J. **1**:887 (May 14) 1932.

The pedigree presented, of which the author speaks as small and incomplete, shows five persons with true epilepsy in twenty-five descendants of family *B*, in three generations. There was also evidence of neuropathic manifestations. In this pedigree the age of onset varied from 8 to 40 years.

FERGUSON, Niagara Falls, N. Y.

APPLICATION OF ANGIOSCOTOMETRY IN THE STUDY OF OCULAR LESIONS OF NASAL SINUS ORIGIN. J. EVANS, Ann. d'ocul. **169**:717 (Sept.) 1932.

Evans points out that careful study of the size of the retinal arteries with small test objects, preferably with the stereocampimeter, elicits important early signs of involvement of the optic nerves in diseases of the nasal accessory sinuses.

BERENS, New York.

CHOREA IN THREE CHILDREN OCCUPYING THE SAME BEDROOM. R. G. WALKER, Brit. M. J. **1**:282 (Feb. 13) 1932.

This is a report of three cases of chorea occurring in three children occupying the same bedroom and supporting the contention that rheumatism may be contagious under conditions of overcrowding.

FERGUSON, Niagara, Falls, N. Y.

MENINGITIS AND SEPTICAEMIA DUE TO MORGAN'S NO. I BACILLUS. ROBERT SILLINS and J. C. HAWKSLEY, Lancet **1**:222 (May 14) 1932.

Two cases of meningitis and septicemia due to Morgan's bacillus are described. The patients, both children, had had no contact, as they came from different towns many miles apart. No cases other than these have been reported.

BECK, Buffalo.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Jan. 19, 1933

PERCIVAL BAILEY, M.D., *President, Presiding*

ATTACHMENTS OF THE DURA MATER TO THE CRANIUM. DR. A. EARL WALKER (by invitation).

In this study the attachments of the dura have been investigated by stripping the dura from the skull in a series of routine necropsies performed at the Billings Hospital of the University of Chicago. In the midline of the anterior fossa the dura is firmly adherent to the crista galli, the foramina for the olfactory nerves anteriorly to the midline of the skull forming an attachment for the falx cerebri and superior sagittal sinus. About the optic nerve it forms a sheath and, entering the optic foramina, merges with the periosteum of the orbit. In the middle fossa the main attachments to the skull are about the nerves and vessels entering and leaving the cranium by the superior orbital fissure, and the foramina rotundum, ovale and lacerum. The juga cerebrales afford a less firm attachment. Along the basisphenoid and around the margins of the foramen magnum the dura is very adherent. It forms a sheath about the acoustic and facial nerves and the ninth, tenth and eleventh nerves, becoming firmly adherent to the walls of the internal acoustic meatus and the jugular canal. At the sites of the venous sinuses of the posterior fossa—the transverse, sigmoid and superior and inferior petrosal—there is a less firm attachment to the inner table.

INTRASPINAL DERMOIDS AND EPIDERMOIDS, WITH REPORT OF A CASE. DR. SIDNEY W. GROSS.

The case is that of a white man, aged 44, who came to the University of Chicago Clinics in May, 1930. The illness began with pain in the left shoulder in 1929, which was followed by weakness and stiffness in this joint and, at about the same time, by moderate weakness in the left leg. Examination revealed atrophy of the left deltoid, biceps and triceps muscles; limitation of movement of the left shoulder; weakness and atrophy of the left thigh, leg and foot; equal and normal reflexes, and an indefinite level for pinprick at the tenth dorsal dermatome. There was no evidence of block with the Queckenstedt test. The spinal fluid was clear; it contained 4 cells per cubic millimeter, and the total protein content was 74.3 mg. per hundred cubic centimeters. Roentgenograms gave normal findings.

In June, 1930, there were increased reflexes, with ankle clonus in the left leg and an indefinite sensory level at the seventh dorsal dermatome. By August the sensory level had reached the fifth dermatome and was definite. There was also a vasomotor level at the fifth dorsal dermatome.

On Sept. 2, 1930, Dr. Bailey removed the laminae of the third, fourth and fifth vertebrae. A tumor was seen at the level of the intervertebral disk between the second and third dorsal vertebrae to the left of the cord, with a posterior root coursing over it. The tumor projected into the cord to a depth of 4 or 5 mm. It was easily separated everywhere except at one point in the lower part, where it was firmly attached. Postoperative recovery was uneventful. In December, 1932, the reflexes in the left leg were still exaggerated, and there was marked loss of all forms of sensibility from the fourth to the eleventh dermatomes and slight loss below the eleventh dorsal.

Histologically, the tumor presented an appearance typical of an epidermoid cyst.

DISCUSSION

DR. PETER BASSOE: I can add another case from the literature. Michelsen, a German, wrote two articles. In the first he warned against the use of spinal anesthesia without ascertaining whether the cord is in good condition and reported the case of a woman who had had an operation for a disorder of the upper abdominal region. Shortly afterward signs of a lesion of the cord developed. A laminectomy was performed in which a tumor of this type was removed. Later, Michelsen wrote on cholesteatoma of the spinal cord (*Deutsche Ztschr. f. Nervenh.* **127**:123, 1932).

STUDIES ON THE TONUS OF HUMAN SKELETAL MUSCLES: THE THEORY OF PARALLELISM OF THE MUSCLE FIBER AND THE SENSORY END-ORGAN AS AN EXPLANATION OF THE LENGTHENING REACTION. DR. PAUL C. BUCY and DR. DOUGLAS N. BUCHANAN (by invitation).

An analysis was made of the facts on which the theory of autogenous inhibition rests as the explanation of the lengthening reaction. Among other facts it was shown that there is no direct experimental evidence of the existence of autogenous inhibitory impulses. Proof of this and an explanation of the absence of any alteration of the central excitatory state during the period of relaxation after the heightened tension seem essential to the theory of autogenous inhibition. Tracings of the changes in the tension of human skeletal muscle during the lengthening reaction, made in the neurologic laboratory of the University of Chicago with a modification of the machine devised by Schaltenbrand, seem to show that the lengthening reaction can be explained on the theory of parallelism of the muscle fiber and the sensory end-organ, and that such an explanation more fully and more accurately explains the observation than does that of autogenous inhibition.

DISCUSSION

DR. LEWIS J. POLLOCK: It is stimulating to hear a report on a phase of study of the tonicity of muscles which has, I think, long baffled every one and has never satisfied even Sherrington, who found it difficult to correlate from his material a similar explanation for both the shortening and the lengthening reaction. In this study one is confronted with the same difficulties as in the study of muscle tone in general; it is concerned a great deal with nomenclature and meanings. Originally the lengthening reaction was described in relation to decerebrate rigidity; whether the phenomena observed in man as the result of lesions of the pyramidal tract correspond to those described by Sherrington remains to be seen. I have never been able to accept the theory that the lengthening reaction is due to inhibition in the muscle, and wish to point out some of the possibilities in the so-called lengthening reaction in decerebrate animals. If the lengthening reaction means the capacity of a muscle to remain stretched to a new length, it appears to me, from the the work of Dr. Davis and myself, that many factors may enter into the formation of this reaction. We thought that the lengthening reaction of a muscle is not due entirely to the inhibitory relaxation of a muscle intoned by a stretch reflex, and found in our studies that a muscle could be stretched to a new length and remain at this new length in completely deafferented extremities. We were able to obtain this result better under the condition of a deafferented extremity. The muscle continued to relax after the maximum of stretch had been applied, so it appeared that it was not a muscle reacting in a graded manner as an elastic substance. Similarly, in the decerebrate animal, after extension was removed there was no corresponding decrement in the muscle. When the animal's head was turned with the occiput down and the muscle was subjected to pull, the latter would assume a new length. If the position of the head was then changed, as the muscle was not fully pulled out, it would again shorten. It seemed to us that if, in a decerebrate animal, extension of the deafferented muscle is followed by its

remaining lengthened and if this is the result of a change in the physical property of the muscle, the muscle should remain indented when it is compressed and the compression is removed. This was shown to be the case. There are factors in the lengthening of muscles in decerebrate animals which we believe cannot be explained by theories other than that of a new molecular formation producing plasticity in the muscle. In a simple experiment by Hill, when sudden stretch was applied to a muscle while the nerve was stimulated, the tension rose rapidly and then fell very slowly to a new level, as though there had been produced in the muscle an increased viscosity so that it no longer acted as an elastic substance. In completely deafferented extremities of decerebrate animals, when a muscle is subjected to extension, a tension curve is developed which corresponds to a substance that is viscid and being extended, not only, as Hill as shown, in the decrement following immediate stretching, but also in the fact that velocity is not developed as in the muscle when normally intoned and not in the decerebrated animal. In this respect the rapidity of stretch bears a close relation to the type of curve that was maintained not only in the muscles but in the artificial models constructed by Hill and in those with which we have been working. The rigidities which we have observed in cases of hemiplegia, in contrast to those of decerebrate animals, have not shown the same type of change in the physical quality of the muscle, but have uniformly given curves typical of elastic substances.

EXPERIMENTAL STUDIES ON THE RÔLE OF THE HYPOTHALAMUS IN THE REGULATION OF BLOOD PRESSURE, WITH OBSERVATIONS ON RESPIRATION. DR. ROY R. GRINKER and DR. LOUIS LEITER (by invitation).

This article will be published in full in a later issue of the ARCHIVES.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTIONS OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, March 7, 1933

BYRON STOOKEY, M.D., *President, in the Chair*

OPTIC PSEUDONEURITIS AND PSEUDOPAPILLEDEMA. DR. ROBERT K. LAMBERT and DR. H. WEISS.

This article was published in full in the September, 1933, issue of the ARCHIVES, page 580.

DEMONSTRATION OF AN APPARATUS FOR ESTIMATING CHRONAXIA FOR CLINICAL USE. DR. KARL M. WALTHARD, Zurich.

In electrophysiology, chronaxia is essentially the expression of the duration of time that an electric current of the double threshold intensity—the rheobase—must act in order to produce a minimal muscular contraction. Bourguignon constructed the first clinical apparatus for estimating chronaxia. It is somewhat complicated and offers difficulties in application. For these and other reasons, the apparatus for estimating chronaxia which I describe was constructed.

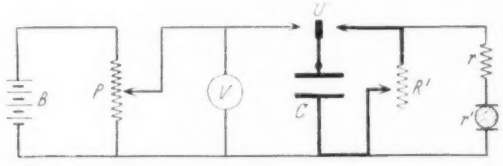
The apparatus is designed primarily for clinical use; it is transportable and can be connected with the usual alternating house current. The alternating current is changed by a special transformer into a direct current not exceeding 200 volts and 80 milliamperes.

The principle underlying the use of the apparatus is simple. Its construction is based on the mathematical formula: T equals C times R ($T = CR$). In this formula, T is time; C, the expression of capacity of a condenser, and R, the

resistance in the discharging circuit of that condenser. T can be estimated by the variation of either factor, C or R. Bourguignon has chosen to vary C by making R constant in the discharging circuit. I vary the R, the resistance, in the discharging circuit of a constant capacity.

The principle of the apparatus is illustrated in the accompanying schema, in which B represents the source of the current, and P is a resistance of 1,900 ohms working as the potentiometer regulating the charging of the condenser C and measured by the voltmeter V. This part of the schema is the charging circuit of the apparatus. In the discharging circuit of the condenser C there is another resistance, R', parallel to the patient's resistance, r', and an additional balancing resistance of 10,000 ohms, r. By the variation of the specially constructed resistance R', the duration of the condenser discharge can be influenced; it can be shortened or lengthened.

To each position of the indicator in front of the apparatus there corresponds a certain amount of resistance in the discharging circuit and therefore also a certain duration of time of the condenser discharge. But, instead of reading the given number of ohms in each position of the resistance R', it is possible to calculate and to estimate empirically the corresponding duration of time of the condenser discharges. This has been done for the apparatus. The indicator on the scale in front of the apparatus therefore indicates the calculated durations of time directly in sigma.



Schema of apparatus for estimating chronaxia.

For technical reasons three condensers of 1, 11 and 149 microfarads are in use. One of the three scales in the front of the apparatus corresponds to each of the microfarads.

In use, it is necessary only to estimate first the intensity threshold of a current unlimited in time. This level can be expressed in volts and milliamperes. I emphasize this point: There exists no specific relation between the two values, as both vary in patients and in time. Then the voltage obtained is doubled by turning an upper handwheel to the right. During this maneuver the patient is insulated by putting the center switch on O. In varying the resistance R' in the discharging circuit by moving a lower handwheel (the center switch being put on "chronaxia"), the chronaxia is estimated when the minimal muscular contraction again appears.

An automatic interrupter is also included. The interrupter, fixed in the apparatus, consists of a glass tube in U form, filled with mercury. One end of the tube is filled with gas which expands under the influence of a heated wire, thus pushing the mercury down until the contact is made on the other side for the condenser discharge. At the same time the heating circuit is interrupted. The gas retracts, and the mercury flows slowly back, reaching the first contact, which closes the charging circuit again. So the charging and discharging of the condenser goes on automatically in more or less regular intervals of from three to four seconds. During these intervals there is sufficient time to get new rates for the stimuli.

The estimation of chronaxia with this apparatus is no more difficult and takes no more time than the older examination for reaction to faradic and galvanic currents.

DISCUSSION

DR. H. G. WOLFF: Dr. Walthard's simple explanation has made clear the principle and purpose of his apparatus. There are certain features I should like

to emphasize. In spite of its bulk, the apparatus is simple. The scale which permits of direct reading is an advantage. The automatic switch which repeatedly discharges the condensers allows the operator to give full attention to the test object and obviates the necessity of manipulating a key.

TREATMENT FOR JUVENILE DEMENTIA PARALYTICA. DR. HOWARD W. POTTER.

Through the cooperation of the New York State hospitals and institutions for mentally defective patients, a study of sixty cases of juvenile dementia paralytica was made possible; thirty-eight patients were treated with malaria or tryparsamide or both, twenty with common arsenicals and bismuth or mercury and one each with radiothermy and diathermy.

Of the twenty patients treated with common arsenicals and bismuth or mercury, seventeen continued to undergo mental and physical deterioration, and several died. Of the thirty-eight patients treated with malaria or tryparsamide or both, the treatment was effective in twenty-seven so far as it prevented further mental and physical deterioration. Five gained a complete, and nine a partial, remission. In the remaining thirteen the condition remained stationary.

Observations on the effect of treatment were made, with two or three exceptions, at least one year after treatment was instituted, and in a great majority of instances a period of from two to five years had elapsed after the beginning of the treatment.

In evaluating the factors that affected the prognosis in the thirty-eight patients treated with malaria or tryparsamide or both, it was found that the prognosis was better in those who prior to the onset of the dementia paralytica possessed a normal mental level, who were in or past adolescence when the symptoms developed, who showed the expansive or confused reaction types and in whom the elapsed time between the onset of symptoms and the initiation of treatment did not exceed two years. Sex, the character of the onset and antisyphilitic treatment prior to the onset of the dementia paralytica did not appear to affect the prognosis favorably or unfavorably.

The treatment of choice in juvenile dementia paralytica is obviously malaria or tryparsamide.

The importance of early diagnosis and immediate treatment with malaria or tryparsamide should be emphasized. It is urged that an examination of the spinal fluid be made in the cases of all children with congenital syphilis and of every child who is mentally retarded or presents one form or another of a psychopathologic condition, when any indication, either in the child or in the family, points to a syphilitic infection.

MALARIA IN THE TREATMENT OF DEMENTIA PARALYTICA. DR. H. C. SOLOMON, Boston.

The results of malarial treatment in 174 cases of dementia paralytica as carried out at the Psychopathic Hospital are presented.

All patients received malarial treatment from one to seven years prior to February, 1932, when this survey was made, and many received follow-up treatment with tryparsamide. Sixty-five, or 37.3 per cent, of the total group of patients are improved and working. An additional 22, or 12.6 per cent, are improved but not self-supporting. This means that practically one half of the patients made a substantial improvement, permitting them to live in the community.

Analysis of the serologic results shows that 35, or 20.7 per cent, have completely normal spinal fluids, and that 29, or 17.1 per cent, have spinal fluids that are nearly normal.

It is shown that not only time but also the amount of subsequent treatment bear an important relation to the serologic results; that is, the longer the time and the more intensive the treatment subsequent to malaria, the more likely is the fluid to be normal, but this is not invariably so.

There is no complete parallelism between the clinical and serologic results, but it is believed that negative tests of the spinal fluid are a necessary criterion for the discontinuance of treatment.

In most instances prognosis as to the result of treatment is not possible. The longevity of patients is greatly increased by malarial treatment. The mortality definitely attributed to malarial treatment is 2.3 per cent.

With malarial treatment, supplemented by tryparsamide and other drugs, the life expectancy of a patient with dementia paralytica is greatly lengthened. One half of the patients so treated may be expected to return to the community and more than one third may be expected to be self-supporting again.

DISCUSSION ON PAPERS BY DR. POTTER AND DR. SOLOMON

DR. LEON H. CORNWALL: The statistical information that these two papers contain is too great to permit of discussion in detail. The attitude taken by Dr. Solomon that malaria and tryparsamide should be combined has always appealed to me as being the proper one. One must understand, of course, that many of the early groups of patients that received malaria were so treated only in order to permit conclusions concerning treatment with malaria alone. I think that it is the general view now that malaria should always be followed by tryparsamide, and that in some cases other arsenical preparations may be indicated later and even an occasional course of bismuth or mercury. It has been my feeling that, since the introduction of tryparsamide and malarial therapy, we have permitted ourselves to create an unjustified bias against the older arsenicals. In making that remark I do not mean that in dementia paralytica I hold my brief for arsphenamine as against t parsamide and malaria or other forms of fever therapy. For instance, in the cases reported by Dr. Potter, sulpharsphenamine was the arsenical that was used in most instances. I consider that this preparation is the most inferior of the arsenicals, and that silver arsphenamine is the arsenical of choice in all forms of neurosyphilis, exclusive of dementia paralytica. It is well tolerated and relatively nontoxic and has the highest index of penetrability to the spinal fluid as indicated by arsenic content. Therefore, I think that possibly some of Dr. Potter's conclusions are a bit unfair to the arsphenamines.

It is my thought that a method of fever production which enables one to use arsenicals at the same time possesses definite advantages. If radiothermy proves to be as efficient as malaria, I think it has a decided advantage, because it enables one to use arsenicals at the same time. Only recently I have had occasion to use a combination of radiothermy and arsphenamine or tryparsamide and the forced drainage method advocated by Dr. Kubie. The patients have had radiothermy every other day, and every five days have been given either silver arsphenamine or tryparsamide, and that has been followed immediately by forced drainage with the intravenous administration of 2 liters of hypotonic saline solution and the withdrawal of from 100 to 150 cc. of spinal fluid.

It is of interest to consider the present attitude concerning the problem of the care of patients with dementia paralytica in comparison with the attitude of twenty years ago, when the intraspinal treatment was first becoming popular. At that time if one reported a favorable result based on a prolongation of the survival period of a patient with dementia paralytica, one was met with an assertion that the diagnosis must have been erroneous because the patient would have died within two or three years. The attitude today is different, as shown by the experience of Dr. Solomon.

The patients who come under treatment early and are treated vigorously have the longest periods of survival. The average period of survival of Dr. Solomon's cases was, I think, about five years. Apropos of that, I saw a patient recently who was treated six years ago with arsphenamine and intraspinous injections. The treatment did not extend over a period longer than six months. Since 1927, no treatment has been given. There has been a partial remission, with an arrest of deterioration; the patient is on a higher level than before treatment, indicating that even inadequate therapy has value.

DR. HENRY A. BUNKER, JR.: In almost every detail my experience has coincided with that of Dr. Solomon. The one respect in which it has differed is that the patients with whom I have worked were for the most part divided into separate groups, some receiving only malaria or only tryparsamide. I do not wish to give the impression that I believe that only one of these agents should be used; rather should I emphasize the truth of what Dr. Solomon has said, that the patient with dementia paralytica needs all the treatment that one can give him, but for reasons which I think Dr. Cornwall has suggested, my associates and I made this division, and in the light of this division I think that the findings which we obtained, especially with regard to the influence of treatment on the spinal fluid, are, if anything, the more striking, in that they were brought about through the intervention of malaria alone, independent of the influence of arsenicals in the great majority of the cases. In these cases the spinal fluid findings came out about as Dr. Solomon reported; namely, after a sufficiently long period complete negativity was obtained in a certain proportion, without any relation, necessarily, as Dr. Solomon carefully emphasized, to the clinical status and outcome. A negative reaction of the spinal fluid was obtained in the latter patients, who were treated only with malaria, after an interval of time following treatment with malaria which ranged up to four years, the minimum period for the obtaining of such a result being two years after treatment with malaria. I think that it is well to bear in mind that treatment with malaria, although it has been shown to be so efficacious and although it is without much question the treatment of choice whatever other measures are used adjuvantly, has what may be called one dubious aspect. I refer to the certain proportion of cases in which a partial remission is secured, with the result that the patient either remains hospitalized for a more or less indefinite period or returns home, but under great restrictions in his activity from a social and economic standpoint, in view of which disabilities he presents an obvious social and economic problem that he would not have presented if nature had taken its course. These cases of partial remission are, as Dr. Solomon has suggested, not always possible to diagnose in advance. The differential diagnosis between the cases which promise well and those which do not is difficult to make. This group of cases in particular, with the added problems, medical and social, that they bring up, gives a definite hint that early diagnosis and earlier treatment are demanded.

DR. CLARENCE O. CHENEY: I wish to emphasize what Dr. Potter has said about our appreciation of the assistance of the superintendents of the state hospitals and schools and of their staffs, who have contributed material to the study he has made; without their cooperation this study would have been impossible. In order to get a larger material than that available at the Psychiatric Institute, we thought it advisable to pool the results from other hospitals. It seems to me that up to the present the attitude toward juvenile dementia paralyica was similar to that noted in connection with the adult form fifteen or twenty years ago, but I think that Dr. Potter's paper has shown that even in cases of juvenile dementia paralytica treatment is indicated, and that it may be well worth while.

Regarding Dr. Solomon's paper, Dr. Bunker's figures presented several years ago gave 2,260 patients with dementia paralytica treated by malaria as compared with 542 treated with tryparsamide. He showed that the results were slightly in favor of the treatment with tryparsamide. Certainly the remission rate was higher when tryparsamide was given than when malaria alone was used (35 per cent as compared with 27 per cent). The question has arisen in some hospitals whether it is advisable or necessary to use malaria when one might get even better results with tryparsamide alone. To such a question we have answered that a combination of malaria and tryparsamide is better, and I gather from Dr. Solomon's paper that that impression is sustained by his figures; he has a definite conclusion that the combination of the two treatments gives better results than either alone. We are not using malaria in the Psychiatric Institute. At present more than 100 patients are being treated by radiothermy. It is too early to report the final results, but thus far we cannot say that the remission rate is so high as in another

series of patients treated with malaria. We are beginning the simultaneous administration of radiothermy and arsenicals, as mentioned by Dr. Cornwall. At present, tryparsamide is given immediately before the radiothermy, in less dosage than if tryparsamide were being used alone. Radiothermy in combination with tryparsamide is given not oftener than twice a week. It is too early to indicate any results. This therapy is based on experimental evidence that in the brains of animals organisms can be removed much more effectively when heat and the arsenicals are administered at the same time. For the last six months we have been following the treatments of radiothermy with tryparsamide, and thus far it seems that the combination of tryparsamide and radiothermy gives better results than radiothermy alone, but the time that this has been tried is too short to permit any definite statement.

DR. H. G. WOLFF: Will Dr. Potter comment on the relation of the remission to the nature of the spinal fluid, and will Dr. Solomon comment on the incidence of spontaneous remissions, particularly in overactive and expansive dementia paralytica?

DR. THOMAS K. DAVIS: It seems to me that Dr. Solomon's figures would be more valuable if one knew the influence of sex on the remissions. Much has been written that suggests that dementia paralytica in the male is different from that in the female. In making an early attempt at prognosis, does Dr. Solomon take into consideration the external bodily configuration to any extent? I feel confident that in a certain kind of thick-necked, dark-haired and hypertrichotic, so-called "adrenal type," dementia paralytica runs a much more malignant course than it does in the person of the type of status thymicolymphaticus. The latter stands a good chance of having a benign form of the disease, with remissions more easily achieved. Does Dr. Solomon's experience bear out this point?

DR. LAWRENCE S. KUBIE: Dr. Solomon has justly emphasized the difficulty of estimating what the chances are of a patient's doing well or badly. I believe that this is the most difficult differential diagnosis in the whole problem of dementia paralytica: the differentiation between a true deterioration or dilapidation and a state of low grade chronic delirium. There are delirious states in dementia paralytica, with or without striking mesodermal components, and apart from the rare Korsakoff pictures. These delirious states are easily recognized when they are florid, and their relatively benign course is predictable. But when they are not so florid, the differentiation is extremely difficult to make between a true permanent deterioration and the low grade, slightly confused deliria, which may clear either spontaneously or under treatment after running a slow course. I wish to know what suggestions Dr. Cheney, Dr. Solomon or Dr. Potter has to make with regard to the problem of diagnosis.

DR. H. C. SOLOMON: I should like to lock horns with Dr. Cornwall on the question of the various arsenical preparations, and with Dr. Cheney on the question of the spinal drainage and hypotonic solutions and all that, because for almost a decade prior to the introduction of tryparsamide we used all of these methods. I have written several papers on this aspect of the subject and discussed the question here in New York. My associates and I used arsphenamine in doses of from 0.6 to 0.9 Gm. twice a week. For a period of months we used spinal drainage, hypotonic solutions and intraventricular, intracisternal and intraspinal injections and spinal drainage, and the best figure that we could obtain in the way of remissions was 10 per cent, as against the 50 per cent or better reported here. I also have in mind a good many patients who have had adequate treatment with the arsenicals and have done extremely poorly, but who have had excellent remissions after being treated with fever and tryparsamide. I am so thoroughly convinced of the inadequacy of those methods as compared with malaria or other types of fever and tryparsamide that I do not believe that they are important. At the beginning of the use of tryparsamide we also used arsenicals and spinal drainage with tryparsamide, and we were not able to see that a combination of the treatment made the slightest difference in a fair group of cases. I do believe

that there are better methods of handling the situation than we are using now, but I also think that arsphenamine, bismuth and mercury are pretty nearly useless when it comes to treating deep-seated syphilis of the central nervous system. Dr. Potter's figures show the inadequacy of these drugs. I doubt whether they are worth using. I think that the damage done to the organism by administering metals which do not do much good is probably worse in effect than leaving the patients untreated. In line with this reasoning Dr. Cheney spoke of the use of tryparsamide with fever, or, I suppose one might say, the use of arsenicals with fever. As far as tryparsamide is concerned, it can be given at the same time as malaria. It does not stop the action of the malaria.

Tryparsamide is not an antiplasmodial or antispirochetal drug. It does not kill the spirochetes of rat-bite fever. Yet it has a most amazing effect when the central nervous system is involved, and I think that that effect is probably not due to a wholly specific effect on the spirochete. I shall give just one illustration. If one inoculates a person with rat-bite fever subcutaneously, there appears a chancre which grows to a huge size as long as the disease progresses. If one gives some arsphenamine, the rat-bite fever is cured, and the lesion heals. If one gives tryparsamide, the lesion heals just as quickly but the fever does not decrease. There is an extraordinary reaction to tryparsamide, but it has no effect on the spirochete at all. What its action is remains to be determined. Stokes tried various methods of producing fever, by colon and typhoid vaccines, and gave tryparsamide at the height of the fever; I think that his results did not show that the combination was better than fever without tryparsamide, or tryparsamide without fever. Theoretically, it is obvious that if we are dealing with an arsenical effect it ought to work better at a higher temperature, but I am not so sure that the arsenic operates as arsenic. I do not believe that we know what goes on. Dr. Bunker and Dr. Ferraro have individually given the best demonstration of what malaria alone will do in the treatment of dementia paralytica that has been given—much better than any of the German or Austrian physicians, because their results were much better controlled. Malaria works well, and so does tryparsamide. On the other hand, a good many patients have been treated with tryparsamide for one, two or three years and get well; then they have a relapse or do not respond; when treated with malaria they make an excellent remission, both serologically and clinically. Some patients will do better with malaria than with tryparsamide alone. I am equally convinced that the good results in some patients who had treatment with malaria, followed by tryparsamide, are due to the tryparsamide rather than to the malaria. Time may have been a factor, but I think it was the tryparsamide. Here again it is a matter of two methods in combination being better than either alone. I think that the important group presented consists of patients who have not done well with the combinations; why, I do not know, and that is the crux of the whole problem of the treatment of dementia paralytica. Possibly some would have done better if they had been treated with arsphenamine and spinal drainage.

Going back to what Dr. Cornwall said about treatment with arsphenamine, we have patients who have done well with arsphenamine. I recall the case, which goes back to 1916, of a woman whose disease was arrested with enough deterioration of cells to prove to any one's satisfaction that she had dementia paralytica. She went home and ran the household in a satisfactory way. But successful cases such as these represent a small percentage of our present results. Some reasonably fair results were obtained in pernicious anemia in the old days when arsenic, iron and transfusions were given, but nobody would go back to that method of treatment when there are other methods which are so much better.

Dr. Wolff brought up the question of spontaneous remissions. These occur in a certain number of cases. They occurred, according to different figures compiled before the more recent methods of treatment were employed, in groups in which no treatment was given. From 1 to 10 per cent, and even some reports as high as 15 per cent, were said to show spontaneous remissions. The figures for the hospitals in Massachusetts are about 5 per cent. These spontaneous remissions

practically never last more than a year. Ninety-five per cent of the patients will be back in the hospital within a year, and the majority die within a few weeks or months after coming back to the hospital. In none of these cases is there any change in the serologic findings. One of the cases recalled what Dr. Cornwall said about the subject of dementia paralytica in the old days, viz., that if one said that a patient recovered, some one would say that the condition could not have been dementia paralytica. One of the patients studied in Massachusetts had a good remission without any treatment, but he had a septic finger and was sick for weeks with sepsis and fever; then he got well.

In dementia paralytica it is true that a higher percentage of patients with a manic or an expansive psychosis get well than is the case with deteriorated patients. I presume that the expansiveness goes down a little, and the patients seem better. I do not know much, if anything, about the body types of these patients. That is a matter which we have thought of studying, but we have not had the energy or the time to carry it out.

As to the sex in this group of 174 patients, only 9 were women. The reason for that is the limitation of facilities in hospitals, so that we have not given malaria often to women, and the incidence of good results in this particular 9 seems to be a little less than in men. The literature has indicated that the percentage of improvement in women is better than in men.

Dr. Kubie brought up the question as to what is meant by deterioration, confusion and so on. That is a psychiatric problem of great interest. I do not know what is meant by deterioration or dementia, except that the persons who never get well are called deteriorated or demented; if they get well, I suppose that they had a pseudodeterioration. A good many patients who have tumors of the brain or deliria appear to be demented; then they get better and are obviously not demented. A certain number of the patients fall into the group with minor deliria; they get well promptly. Some of the situations arising both spontaneously and under treatment are striking. A patient enters the hospital with a psychosis lasting for several weeks; at the end of from three to five days in the hospital he seems to be in fairly good condition; in some instances the patients have been drinking too much alcohol, and the psychosis is an alcoholic one; in other cases this is not so, but they get well or make a symptomatic improvement for some reason or other, which may or may not have had anything to do with the treatment.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

TRACY J. PUTNAM, M.D., *Secretary*

Regular Meeting, March 16, 1933

E. S. ABBOT, M.D., *Presiding*

MELANOBLASTOMA OF THE LEPTOMENINGES. DR. J. KASANIN and DR. R. P. CRANK.

History.—C. E. T., a man, aged 48, was admitted to the State Hospital for Mental Diseases at Howard, R. I., on Jan. 10, 1933. The patient's mother became psychotic at the time of his birth and was committed to an institution for mental diseases. A maternal uncle was a patient in a hospital for mental diseases. The patient was born on Feb. 13, 1884. Because the mother was mentally ill at the time of his birth he was taken care of by the paternal grandmother. He was a sickly baby. He was a nervous, temperamental child, high strung and addicted to temper tantrums. Adolescence was normal. He was a hard working, diligent person who, however, showed rather poor judgment in work. In spite of extreme

effort he was barely able to make a living on his farm. He had always been in good health until eight years prior to presentation, when there developed a mild psychosis with ideas that he was very sick, had to be operated on and was persecuted by an imagined enemy. This lasted for a few weeks. He was in the Rhode Island Hospital where it was advised that he should be committed to a hospital for mental diseases. The family took care of him at home, and within six months he was his usual self. Since then he had had two or three short mental upsets which were characterized by somatic delusions. The patient was a "lone wolf." He took care of the farm, and his chief interests were hunting, driving teams and taking care of the cattle. About three months before presentation he complained of a small pigmented mole between his shoulders. He was advised to tie it with string, which he did; it helped him.

Three weeks before admission the patient began to complain of severe pains in the back of the head and shoulders and said that he did not feel well. He appeared ill; his color was poor, and his eyes were inflamed. He seemed to be drowsy and mentally slow. Three days before admission he was mute, apathetic and occasionally restless; this condition gradually merged into a stupor.

Examination.—On admission he was in a state of stupor; the face and neck were deeply flushed; he did not respond to questions and resisted any manipulation. A few rhythmic twitchings of the left arm were observed. On physical examination the only thing of note was a raised, pigmented mole close to the midline at the level of the inferior scapular border. The urine was normal. A blood count showed 11,300 white cells, with 75 per cent neutrophils and 2 per cent myelocytes. The blood and spinal fluid were essentially normal. There were 4 cells in the spinal fluid; the Pandy and Ross-Jones tests were positive, 1 plus.

Neurologic examination showed nothing unusual, with the exception of the stupor. There were dysarthria, slurring of speech and, probably, aphasia, but the stupor was so profound that this could not be studied. There were no pathologic reflexes. The disks were normal.

Course.—The condition improved somewhat. The patient began to sit up in bed, occasionally walked in the ward and at times was able to utter a few sentences. He was, however, confused. On January 23, he lapsed into profound stupor again and had convulsions which consisted of marked twitching of the left upper extremity, suggestive somewhat of decerebrate convulsions. He was rigid; the abdominal reflexes were not obtained, and there was a bilateral Babinski sign. Tuberculous meningitis was thought of, but a second lumbar puncture showed only 5 cells with a total protein of 51 mg. per hundred cubic centimeters. Various attempts to stimulate the patient did not succeed. The stupor became more prominent; the bilateral Babinski sign persisted and together with this there appeared a total bilateral ophthalmoplegia. The patient died on January 27, seventeen days after his admission to the hospital.

Autopsy (R. P. Crank).—The body was somewhat emaciated. In the left interscapular region was an elevated pigmented nevus, 1.5 cm. in diameter. About the nevus was a bluish discoloration which faded into the tissues about 1 cm. from the edge of the tumor. No pigmented areas were found in the skin. No enlargement of the regional lymph nodes was found. The lungs were dotted with brown nodules, varying in size from 2 to 8 mm. and in color from light to dark brown. Similar nodules were scattered throughout both lungs, being more numerous about the hilar regions and on the pleural surfaces. The lymph nodes of the lungs and hilus were uniformly enlarged, brown and firm in consistency. The left lung weighed 405 Gm., and the right, 350 Gm. The mediastinal lymph nodes were enlarged, firm and brownish black, and varied from 1 to 2.5 cm. in diameter. There were also other scattered nodules in the mediastinum, apparently not related to the lymph nodes. The parietal pleura was entirely free from nodules. There were scattered small brown nodules in the parietal pericardium. The heart was grossly normal. Below the region of the diaphragm not a single suggestive nodule was found.

The leptomeninges were diffusely infiltrated with a firm, dark brown tumor growth which extended over the entire length of the brain and spinal cord. There was some cortical invasion which varied in degree in different areas.

Microscopically, the cells of the primary tumor varied in size and shape from a very large clear cell, many of which contained abundant pigment and a few of which showed mitoses, to a small or denser type of cell varying from polygonal to spindle shape. The nuclei were hypochromatic. Occasional multinucleated cells were found. The metastatic process in the lungs, lymph nodes and meninges was composed chiefly of larger clear cells, with rather abundant pigment, with an occasional mitosis and multinucleated cell. There was a definite tendency toward invasion of the cortex along the perivascular spaces, associated with hyaline changes in the walls of the vessels.

Diagnosis.—This was: (1) primary melanoblastoma of the skin; (2) diffuse melanoblastoma of the leptomeninges, brain, lungs, mediastinum and pericardium.

ALZHEIMER'S DISEASE. DR. J. KASANIN and DR. R. P. CRANK.

History.—C. A. M., a man, aged 49, a widower, was admitted to the State Hospital for Mental Diseases at Howard, R. I., on May 12, 1932, by transfer from the Psychopathic Division of the Charles V. Chapin Hospital. The family history was without significance. The birth and early development were normal. The patient completed grammar school at the age of 16, and then took evening courses in free-hand drawing. This study was financed by a scholarship received on account of artistic ability. He worked at various jobs. For eighteen years before admission he worked as a lithographer. He married at the age of 31, and his married life was happy. There were no children. The wife died when the patient was 43.

The patient had always been a happy, sociable person, who spent the evenings in the family circle, talked a good deal, sang and indulged in other simple recreation. At the age of 45 his behavior changed a great deal. He began to feel sleepy most of the time. He would come home from work, sit down and fall asleep in a chair. At the same time, his employer noticed that he was not as efficient as he had been; he took no interest in his work; he appeared to be confused and very quiet; he paid no attention to co-workers with whom he was on friendly terms, and he dropped a job before he finished it. The firm retained him for over a year, hoping that he would get better, but finally had to discharge him. On leaving his position he became more sleepy and spent most of the day dozing in a chair. When his wife died in 1929, the patient was so confused that he was entirely incapable of making plans for the funeral.

Three years before admission to the hospital, the father took the patient to live with him and do light housework. This plan, however, did not materialize as the patient was incapable of doing even the easiest tasks. He became entirely dependent on his father. He was not able even to dress himself. When he attempted to do so he would get his clothes into a mess and instead of trying to straighten them out, he would lie down and go to sleep. When the father came home he frequently found the patient lying down clad in his underwear, which was either on backward or only half. He was forgetful and could not remember anything that his father told him. On one occasion the father returned from work and noticed an odor of gas. He learned that the patient had turned on the gas-range and forgotten to light the jet. The patient complained of feeling ill and was aware that something was wrong with him. He thought that a little girl was planning a scheme to arrest him.

The patient was admitted to the Psychopathic Division of the Charles V. Chapin Hospital on Aug. 4, 1930, where he stayed for a week. He seemed very dull; there was psychomotor retardation. He expressed no delusions or hallucinations. Memory was poor, and speech was drawling and indistinct. On August 28, he was sent to the Dexter Asylum. While there he caused trouble by being restless, pulling at the bed clothes, soiling himself and taking off his clothes. He annoyed other patients and was unmanageable.

Examination.—The patient was readmitted to the Charles V. Chapin Hospital on Dec. 8, 1931. He presented a picture of marked mental deterioration evidenced by inability to perform the simple acts or even to take care of himself.

On neurologic examination, the patient's attitude, hypertonicity and loss of associative movements were suggestive of encephalitis; the superficial reflexes also were greatly exaggerated, with loss of the abdominal reflexes. The disks were normal. The blood and spinal fluid were normal. On Jan. 19, 1932, encephalography showed evidence of atrophy in the frontal lobes of the brain. Apparently no air reached the ventricles. The patient was so uncooperative that the roentgenologist refused to make a positive diagnosis. The condition continued to grow worse, and on June 27, the patient was admitted to the State Hospital for Mental Diseases.

There, the patient appeared to be about ten years younger than his age. He giggled and chuckled continually and when asked questions uttered an unintelligible jargon, in which occasionally separate words could be made out, but which consisted for the most part of a rapid repetition of syllables and parts of words. When left in a chair he made purposeless movements, chewing, sucking air through closed lips, plucking at his clothes, whistling, rubbing his palms over his thighs or fumbling with the toes of his slippers. Twitchings of the muscles of the trunk and upper extremities were noted. The mood was one of euphoria, especially when he was addressed. When questions were pressed, he would say, "Come on back, I didn't take any—where are you walking," and give other meaningless answers. Once when the knee jerks were examined he suddenly straightened up, swore and asked abruptly, "What are you trying to do?" He showed obvious echolalia; when asked how old he was, he said: "45, 46-6-6-6-." An interview would usually consist in the patient's repeating the questions asked and emitting bursts of laughter; he would imitate the examiner's voice and questions asked, repeating them innumerable times. This usually discouraged further attempts at examination. It was impossible to determine his intellectual functions, but it was obvious that he suffered from a profound dementia.

Neurologic examination, made on May 19, revealed occasional twitchings of various groups of muscles in the extremities. The cranial nerves were normal. There was a marked play of facial muscles. The optic disks and vessels were normal. The knee and ankle jerks were very active. The abdominal and cremasteric reflexes were not obtained. There was a question of a Babinski sign on the right. The urine was normal; the white cells of the blood numbered 10,300; the red cells, 4,600,000; the hemoglobin was 75 per cent; the blood sugar, 83 mg.; the nonprotein nitrogen, 27 mg. The spinal fluid was clear, without cells, and the colloidal gold test was negative. Films of the skull were not satisfactory. Examination of the disks, made on June 14, showed blurring on the upper nasal side.

On July 12, the patient had a seizure, which was followed by a semicomatose condition. He recovered from this, but again became stuporous on July 14, when examination revealed congestion of the right lung, with dulness and râles. On July 15, the patient died.

Autopsy (R. P. Crank).—The autopsy was performed within two hours after death. The body was somewhat emaciated, with generalized symmetrical muscular atrophy. There were no contractures. There was bronchopneumonia of the lower two thirds of the right lung. The left lung was normal. The heart was grossly normal. The liver was of normal size, possibly slightly enlarged, and contained a large amount of fat. The spleen was slightly congested. The kidneys were essentially normal. The stomach and intestines showed no gross lesions.

There was no noticeable thickening or discoloration of the dura. The leptomeninges were of normal appearance. The vessels showed no gross evidence of sclerosis. The brain presented a striking picture of symmetrical atrophy. Both frontal lobes were markedly atrophic, the maximum atrophy being in the superior frontal gyri. The sulci of this region were widened and filled with fluid. The precentral gyri stood out rather prominently and appeared to be well preserved grossly. Both temporal lobes showed atrophic changes. The inferior temporal

gyri were shrunken and appeared moth-eaten, with less severe atrophy in the middle and inferior gyri. Of the two temporal lobes, the left appeared much more atrophic than the right. The parietal lobe showed symmetrical atrophic changes, with shrinking of the gyri and widening of the sulci. The occipital lobes showed a much less severe degree of atrophy than the other portions of the brain. The hippocampal gyri showed definite but not severe atrophic changes. The brain was very soft and suffered some distortion in handling. The weight of the entire brain was 1,197 Gm. The cerebrum alone weighed 987 Gm. (The weight of the right hemisphere was 524 Gm., that of the left hemisphere, 463 Gm., and that of the cerebellum, pons and medulla, 210 Gm.)

Histologic Examination of the Brain: Cellular stains of cortical regions revealed a marked dropping out of cells, especially in the superior frontal and superior temporal gyri, with similar but less marked changes in the middle and lower frontal and temporal gyri and in the parietal regions. No definite changes were noted in the precentral, occipital and hippocampal regions. The general architecture seemed normal.

Bielschowsky preparations revealed numerous senile plaques in the frontal, temporal and parietal regions, with scattered plaques in the precentral and occipital regions. These were limited largely to the cortex. The cells of the cortex showed striking changes in the neurofibrils, varying from thickening and increased stainability to advanced alterations in which the fibrils were thickened, forming a network or shell about the former cell bodies, leaving little but the argentophil framework. These cell changes were found in all regions of the cortex. They were more striking in the superior frontal gyri, with slightly less extensive involvement of the other frontal, temporal, parietal and postcentral regions, and much less marked in the occipital and precentral regions.

Gold sublimate stains showed a definite increase in the astrocytes throughout the cortex and in the caudate and lenticular nuclei. Hortega stains showed numerous plaques in the cortical areas mentioned and also in the hippocampal gyri and midbrain nuclei.

The symmetrical atrophy, together with the histologic findings of senile plaques throughout the brain and changes in the neurofibrils corresponding to those described in Alzheimer's disease, and also the clinical data establish this as a case of Alzheimer's disease.

DISCUSSION ON PAPERS OF DR. KASANIN AND DR. CRANK

DR. DAVID ROTHSCHILD: The age at onset was less than that usual in Alzheimer's disease. The mode of onset was atypical and suggested encephalitis. Senile plaques do occur in some of the subcortical ganglia, but they have seldom been described in the thalamus. It would be of interest to know whether some of the gray nuclei surrounding the third ventricle showed changes. The peculiar affective changes were probably due to frontal lesions. On the whole, the clinical picture did not bear any resemblance to that of senile dementia. This case lends support to the view that it is no longer justifiable to regard all cases of Alzheimer's disease as atypical examples of senile dementia.

DR. J. B. AYER: I observed a case associated with a small pigmented mole on the arm. It was said not to have changed in size, shape or character for ten years, yet on excision it showed numerous mitotic figures. At postmortem examination one large lesion was found which had caused hemianopia and aphasia. There were also multitudinous minute lesions under the pia. One interesting thing was that the metastatic lesions were not melanotic.

DR. C. L. KUBIK: The cells of the metastatic nodules were much like those of the primary tumor. Some were pigmented and some not, a common finding in the melanomas. Curiously, no metastatic lesions were found in the lungs or other organs of the body. The axillary lymph nodes were not enlarged. In another case there were a large melanotic tumor and numerous small ones in the brain,

and a very small tumor of the lung. In view of the fact that primary melanotic tumors are not found in the lung, it may be that the large tumor of the brain was the primary growth.

DR. J. KASANIN: We thought that the mole was the primary lesion. A tumor of the same type has been described by Farnell as a primary melanosarcoma of the brain. In response to Dr. Rothschild, it was due to specific lesions in the basal ganglia.

DR. R. P. CRANK: The lesion on the spine was a congenital mole and was tied because it was growing and had been giving some trouble. My belief is that that was the primary tumor, although it is possible that the primary one was in the meninges.

TECHNIC OF ENCEPHALOGRAPHY, WITH DEMONSTRATION OF A NEW APPARATUS. DR. H. C. SOLOMON, DR. S. H. EPSTEIN and DR. S. S. HANFLIG.

At the Boston Psychopathic Hospital, in order to mitigate the severity of the reactions during and after the injection of air and to make the encephalographic procedure less disturbing for both the operator and the roentgenologist, we make use of the nonvolatile anesthetics such as pentobarbital-sodium, amytal and avertin. We give an intravenous injection of from 5 to 7½ grains (0.324 to 0.492 Gm.) of pentobarbital-sodium dissolved in from 10 to 15 cc. of distilled water. The solution is injected in from three to five minutes. The patient is usually in a state of narcosis by the time the injection is completed. Occasionally a subcutaneous injection of ¼ grain (0.016 Gm.) of morphine sulphate is given fifteen minutes before the pentobarbital-sodium. Complete anesthesia is obtained in from ten to twenty minutes after the injection, and the patient is then ready for the encephalographic procedure. As the patient is in a state of muscular relaxation, it is convenient to have an apparatus that will hold him in position for the injection of air and the roentgenographic procedure. This apparatus (shown in lantern slides) was designed by Dr. S. S. Hanflig, whose technical skill has contributed much in the field of orthopedic surgery. During the induction of anesthesia the patient is held in the apparatus in a recumbent position. He is then brought to an upright position by a ratchet and sliding device and held securely by the head piece and abdominal and shoulder straps while the lumbar puncture is being done. Various angles of the sitting position may be obtained. This is important for the injection of air, because it facilitates filling of both the subarachnoid space of the head and the ventricles. By means of the movable head piece changes in the position of the head may be made by adjustment of the screw handles. This insures complete emptying of the cerebrospinal fluid system and replacement by air. The lumbar puncture and the injection of air are made through a rectangular opening in the back of the chair. We use the two-needle method, allowing the fluid to escape from the lower needle and injecting the air by means of the upper needle.

When the injection of air is completed, the patient is wheeled to the x-ray room in the sitting position. The roentgenograms are made with the head in the erect position by merely shifting the chair around in relation to the x-ray plate which is suspended vertically.

This technic is of a special advantage in dealing with psychotic, disturbed or fearful patients. During the injection of air the patient is completely anesthetized; the operator is not disturbed by complaints; nausea and vomiting do not occur, and there is practically no diaphoresis. The roentgenograms are made with the head in any desired position; no vomiting occurs as is frequently the case when an injection of air is performed without anesthesia, and the roentgenologist has no interference with his technic. The narcosis gradually wears off in from four to six hours. On awakening the patient rarely has a complaint and usually is able to take nourishment. As a rule there are no headache, gastro-intestinal symptoms or fever.

DISCUSSION

DR. E. DE THURZO: It is difficult to say which is the better way, lumbar or baso-occipital puncture. Many prefer suboccipital puncture. It is not necessary to inject so much air; from 70 to 80 cc. of air gives a good x-ray picture; from 100 to 200 cc. makes it very unpleasant for the patient. Another question is whether it is useful to use narcotics. We do not use them much in Europe, at least not such deep narcotics.

DR. A. H. RUGGLES: It is possible that encephalography should not be attempted without the opportunity of proceeding with neurologic surgical intervention. We have used avertin with most satisfactory results. The roentgenograms have been taken with a portable machine and with the assistance of trained people to secure posture and changes of posture by direction. The results are satisfactory. Encephalography should be attempted only with assistants who are conversant with what they are doing.

DR. W. J. MIXTER: Encephalography is at times of great value in neurologic surgical procedures. I believe in injecting air into the whole of the ventricles and subarachnoid space when it can be done, instead of only partially filling them. I do not believe that this can be done satisfactorily with 25 cc. of air. It seems to me that the apparatus shown marks a distinct advance. I believe that a hospital should secure the best apparatus possible to insure success, and I think that the apparatus shown here is good.

DR. J. B. AYER: I think that we secure adequate filling by the method we use even without the chair. The narcosis or anesthesia could be much better than that we use. We have tried using small amounts of air and have found the result unsatisfactory; we do not secure as good a filling with cisternal as with lumbar puncture. The method described seems to allow one to inject the full amount of air and to obtain results which are not obtained when the patient is not in complete narcosis.

DR. J. KASANIN: Is this depth of narcosis necessary for encephalography? When 100 cc. or more of air is injected, the reaction on the patient is so strong that I do not like to use as much.

DR. H. C. SOLOMON: The device is not very elaborate and cannot shake the patient. Incidentally, the chair was built at the Massachusetts General Hospital.

DR. S. H. EPSTEIN: We believe in filling the whole of the ventricular and subarachnoid systems. We do use a deep anesthesia, but by means of the narcosis the operation is much simplified and postoperative symptoms are entirely eliminated. The narcosis not only is important from the standpoint of avoiding reactions, but is well suited for the manipulation of patients, especially those of the psychiatric group.

ORGANIC FUNCTIONS IN SCHIZOPHRENIA. DR. R. C. HOSKINS and DR. F. H. SLEEPER.

This article was published in full in the July, 1933, issue of the ARCHIVES, page 123.

DISCUSSION

DR. K. BOWMAN: The pulse rate was very low at the time when the basal metabolic rate was taken as the patient was breathing pure oxygen. Was this an indication of slower breathing? The variability of the output of urine would depend on the amount of liquid ingested or on variability in the patient himself. Was that left entirely to the patient?

DR. R. G. HOSKINS: Breathing of oxygen does not slow the pulse rate significantly. These figures have been controlled with results on normal persons treated in the same way. In regard to the urinary volume, there was no therapeutic forcing of fluids. Therapeutic measures were omitted during the seven months.

Book Reviews

Third Report of the Miners' Nystagmus Committee. Medical Research Council, Special Report Series, no. 176. Price, 9d net. Pp. 36. London: His Majesty's Stationery Office, 1933.

This is the third of three reports from the Medical Research Council, published on the recommendation of the Committee on Miners' Nystagmus. The two previous reports appeared in 1922 and 1923, respectively. The Committee on Miners' Nystagmus consisted of Prof. M. Greenwood, chairman, Prof. E. L. Collis, Millais Culpin, J. S. Haldane, L. Isserlis, T. L. Llewellyn, Sir John H. Parsons and Air Vice-Marshal Sir David Munro, secretary.

The principle finding of the earlier committee was that the chief symptom of miners' nystagmus, namely, the involuntary oscillation of the eyeballs, was caused by an insufficiency of light reaching the eye of the miner while at work. It was assumed that the most important of the measures of prevention was to secure adequate illumination for the miner while at work. The present committee, in this third report, reaffirms in the strongest terms both this scientific conclusion, and its practical corollary.

In view of the fact that since the publication of the early reports there has been no reduction in the burden of disability assigned to conditions officially certified as coming under the heading of "miners' nystagmus," they (the committee) thought it their duty to investigate further and pay greater attention to the general symptomatology of the disease as recognized for compensation. This has led them to a more extended examination of the nervous or psychologic factors which must play a part in the production of industrial disability, a subject which was by no means ignored by their predecessors. The conclusion is reached that the criterion of incapacity is not easily determined. On the one hand, oscillation of the eyeballs per se is not a trustworthy test for incapacity, since many men with this symptom are working efficiently. On the other hand, the absence of this symptom in the presence of symptoms of a nervous or psychologic kind is not sufficient proof of fitness for work.

The members of the present committee, therefore, have had to accept the inherent inconsistencies in the symptomatology and to content themselves with drawing attention to these, leaving to the administrative departments consideration of the action to be taken on the facts set out. Of these, the most important, in the opinion of the committee, is that the true significance of the various symptoms presented by sufferers from this complaint can be elucidated only by medical men with the requisite training.

In 1908, Great Britain had 783,000 coal miners employed below ground. A total of 460 persons, with both old and new cases, were drawing compensation at that time for miners' nystagmus. In 1930, there were 742,000 miners employed below ground, and a total of 10,638 were drawing compensation. Of these, 7,575 had old cases and 3,066 new cases. Up to 1919, the number of patients with new cases and the number with old cases who remained under treatment were about the same. Since then, the number of old cases has increased in three years to more than 7,000, and has remained about constant. The number of new cases has changed but little, it being lower in 1927, when there were less than 2,000 persons with new cases placed on compensation.

In the subsection of the report wherein the present committee considered the conclusions of the first committee, they called attention again to certain contributory rather than fundamental factors which may also be a factor in the development of miners' nystagmus. Many of them are not new, and discussion of their

etiologic significance can be found in previous reports: effects of errors in refraction, of abnormal posture causing fatigue of the eyeballs, of the spectral quality of the light supplied, of glare and of poisons such as mine gases and alcohol.

In the discussion of illuminating factors, they call attention to certain physiologic and physical data, which are certainly relevant. Besides being capable of seeing objects in a bright light, the human eye also adapts itself for seeing objects in a very dim light. When this power (known as dark adaptation) is enfeebled, the person suffers from so-called night blindness—a frequent early symptom of miners' nystagmus. It is, however, by no means certain that night blindness is always due to loss of dark adaptation, as it may be a nervous symptom (vide infra). In the normal eye in a condition of complete dark adaptation (i. e., when it is kept protected from light for a considerable period) the sensitivity of the central part of the retina is very much less increased than that of the periphery. Hence, under dim illumination, the peripheral parts of the retinal field are used. The critical point at which vision changes over from central to peripheral has been found to be when the intensity of light reaching the eye is 0.0073 of a millilambert or 0.0068 foot-candle, and this critical figure, obtained under the carefully controlled conditions of the laboratory, may be presumed to hold good under the conditions of the coal mine.

It must be remembered that the amount of light reflected into the eye determines clearness of vision. As coal absorbs from 88 to 97 per cent of all incident light, the committee had little difficulty in realizing that the illumination was an important factor. Photometric tests taken under ground with a 2 volt electric cap-lamp gave an average illumination at the coal face of 0.27 foot-candle. They realize that this amount is not constantly attainable, and they considered that an ultimate goal be made out of 0.25 foot-candles on the coal surface. The critical figure of illumination from a laboratory standpoint is being obtained, in that 2 and 2.5 and even 4 volt lamps were being used. They cannot, however, control the factor of varying distances of the hand-lamps from the coal face. In one test 40 men were given lamps of from 2 to 2.50 candle-power, while a control shift, also of 40 men, used the old lamps of from 0.5 to 1 candle-power. Seven men in each group showed oscillation of the eyes at the start of the test. It was found that the men with the better lamps lost their oscillation and subjective symptoms, while there was no improvement among the men of the control group, 9 men showing oscillation at the end of the test.

The investigators also stressed the difference which dirty lenses made in the amount of light emitted by lamps. In some instances the percentage increase in illumination after cleaning was found to be 20 per cent. Evidence was also present that in some instances a certain type of cap-lamp was being used. Lamps of an average candle-power of 3.34 before use, dropped to 1.32 foot candle-power at the end of the shift. On the other hand, in another colliery, of 339 Oldham lamps, tested before use and with an average candle-power reading of 1.29, 260 available for retesting after use gave an average candle reading of 0.95. One can see that, in comparison, these results were highly satisfactory. The committee also considered them as satisfactory.

The committee considered seriously the strong relationship which seemed to exist between certain psychologic factors and the development of miners' nystagmus. They believe that owing to the preexistence of these psychologic factors, a large number of men were receiving compensation wherein this constitutional state is a greater factor than is that of the development of the nystagmus. The three outstanding of these are: (1) psychoneurosis indicating a disturbance of mental reactions, fears, depressions, inhibitions and impulses, for example, or of altered behavior, such as irrational conduct, and the production of pseudophysical symptoms as exemplified by the bodily phenomena of hysteria; (2) minor psychoses which can be grouped into hysteria, anxiety states and obsessional states, though rigid distinctions are not to be expected and the patient's symptoms can pass from one group to the other, and (3) neuroses in which cardiac dysfunction and digestive upset serve as examples.

The symptoms of miners' nystagmus are divided by the committee into ocular and nervous. Under the ocular signs and symptoms are defective visual acuity, night blindness, photophobia associated with blepharospasm, forced ocular movements and tremors of the head and limbs. Under nervous symptoms are the disordered action of the heart, which is now admitted to be a neurosis in the narrow sense of the word, and neurasthenic symptoms of sleeplessness, headache, depression, claustrophobia, insomnia and that long chain of neurologic symptoms which are so often grouped under the symptomatology of traumatic neurasthenia.

It is of interest that all of these symptoms, even those which are described as ocular, still have a strong neurologic quality. Night blindness, for instance, has often been observed in states of malnutrition, and now its psychoneurotic effect is more commonly recognized. The same thing is true of photophobia, and most ophthalmologists, if faced with a case of photophobia with no ocular abnormality, would unhesitatingly call it hysterical. Tremors of the head and limbs are so generally psychoneurotic that special reference is unnecessary, and so also is the case in forced ocular movements.

The sequence of events in typical cases is of interest. One man was described as saying: "Whilst holing in the coal a blister exploded in my face, my eyes got bad at once and I had to be led out." Another said: "I was buried under a fall, my eyesight failed at once. I had no trouble before." These examples and a consideration of the symptoms that develop in more typical cases show an analogy with the condition once known as "shell-shock." In the latter disorder the assumption, on insufficient evidence, that physical forces produced nervous symptoms was so pernicious in its effects that the phrase "shell-shock" was prohibited; in the other it is not sufficiently recognized that the attribution of nervous symptoms to a physical cause is a probable factor in the evolution of the compensated disease.

In the treatment of the compensation conditions, the committee thinks that it is chiefly the psychologic factors which need attention. The first essential in a satisfactory handling of the incidence of this disease is a better understanding of its nature, and especially of its analogy with that condition once known as shell-shock. The arduous work, the ever-present element of danger and the fear of incapacity are circumstances common to both disabilities, and they are the very circumstances in which an anxiety state is easily set up.

As to what the suitable treatment is, the first step plainly is to combat the belief that the psychoneurotic symptoms present can be a direct physical result of oscillation of the eyeball, for the patient's outlook may well become hopeless when he hears that medical science has nothing to offer in the way of this disorder. From an organic standpoint, the committee are strongly of the opinion that the practical treatment of the disease from an administrative point of view should consist in the elimination of a hopeless dependence on compensation by the provision of opportunities for work of some kind, the end in view being complete restoration to full work under ground, under conditions of proper illumination, even if this has to be preceded by a period of work in daylight.

The abstract given (vide supra) represents the contents of the committee reports. This report is followed by appendixes 1 and 2. The first is an investigation of 36 cases of miners' nystagmus by Prof. Mullais Culpin, a member of the miners' nystagmus committee. The findings in the various cases are summarized in table form. Of the 36 cases, the nervous state was considered as "healthy" in only 6. In the table of the relation of oscillations to nervous symptoms, 22 of the patients who had no oscillation had the highest incident of nervous symptoms. This seems to bear out the statement and recommendation made by Professor Culpin as a result of his examination of these 36 patients. He presents the following general scheme: (*A*) oscillation with no disability; (*B*) oscillation with subjective movement of objects; this appears to be a recoverable stage and may be organically determined; on the other hand, the added symptom may behave as a hysteria and for a time protect against further developments; (*C*) the unfolding of further psychologically determined symptoms—hysterical, anxiety or obsessional, with the oscillation now behaving as a hysterical tremor and tending to disappear; (*D*) the disappearance

of oscillation and the complete development of a psychoneurosis. Culpin expressed himself as follows: Whether there is a disability independent of any psychoneurotic element may be left an open question. One may speculate as to whether the oscillation causes disability only in those men already predisposed to nervous symptoms, but, even if one grants it, the number of such men in all grades of workers is so great that the need for preventing the oscillation still remains. The psychologic effect of "darkness made visible" has not hitherto been stressed, but in the men examined there were sufficient examples to show that this is a likely factor in the stimulation of a pathologic fear of the dark. Apart from the aim of diminishing oscillation there are, therefore, psychologic reasons for a general improvement in illumination, both by better lamps and by such expedients as whitewashing the roadways and other passages in the mine. Improved lighting, however, cannot materially diminish the incidence of the compensated disorder unless, in addition, the true nature of the majority of cases is recognized and both prophylaxis and treatment are directed accordingly.

Appendix 2 is the report of Mr. T. L. Llewellyn relative to changes in illumination of mines and the incidence of miners' nystagmus. The earlier notes of Mr. Llewellyn and his consideration of illumination in 1929 are compared. He discusses in detail the various lamps used, the degrees of illumination of the lamps, the candle-power and his recommendations. Of 950 men examined, 20 per cent showed oscillation. Of these, about 46 per cent were under 30 years of age and constituted 16 per cent of the cases showing oscillation. Those over 30 years of age numbered 54; 84 per cent of the oscillations occurred in this number.

Ergebnisse der Reiztherapie bei progressiver Paralyse. Sonderausgabe von Heft 65 der „Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten". Edited by K. Bonhoeffer and P. Jossmann. Price, 14.80 marks. Pp. 154. Berlin: S. Karger, 1931.

This monograph, edited by Bonhoeffer and Jossmann, contains papers contributed by various writers. Jossmann summarizes the results obtained with *Reiztherapie* (irritation or stimulation therapy) in the treatment of dementia paralytica between 1922 and 1929 in various psychiatric institutions in Berlin. The material includes more than 2,200 cases. Clinical improvement was obtained in more than 40 per cent and practical cure in 23 per cent. No fundamental differences were noted between the therapeutic achievements by different methods of *Reiztherapie*. The reviewed material suggests that early treatment and nonadvanced age offer the best chances for remission.

One will find in Jossmann's article extremely interesting data in regard to various aspects of the problem of *Reiztherapie:* the relation between the therapeutic results and occupation; somatic, blood and cerebrospinal fluid findings, as compared to the therapeutic attainments, malaria therapy and psychopathology of dementia paralytica.

Kallmann emphasizes the usefulness of 1 per cent suspension of sulphur in olive oil as a substitute and complement of malarial treatment. Stating that the principle *nil nocere* has not been fulfilled by the latter, he finds it indicated to attempt treatment for dementia paralytica by fever-inducing means which, above all, have the merit of being innocuous. Sulphur in olive oil proved to be inoffensive in cases of dementia paralytica in which the malaria therapy is generally considered to be a great risk. The drug is recommended for patients over 60 years of age, for those afflicted with cardiovascular and renal diseases and pulmonary tuberculosis, for cases showing signs of low resistance and for the tabetic form of dementia paralytica. Sulphur in olive oil would also be the adequate fever-inducing means in far advanced cases of dementia paralytica. Finally, Kallmann advocates the combination of malaria treatment (four attacks of fever) with sulphur in olive oil (eight attacks of fever). The procedure of treatment with sulphur in olive oil as used by Kallmann is as follows: The initial dose is 2 cc.; this is gradually increased if the temperature remains below 39 C. (102.2 F.). The highest dose

used was 8 cc.; in most cases from 3 to 4 cc. is sufficiently effective; the drug is administered intramuscularly three or four times a week. Kallmann also recommends the combination of sulphur in olive oil with a suspension of bismuth and arsphenamine.

Schwarz discusses the indications for repeated series of fever-inducing treatments and the results which, in the light of clinical experience, are to be expected. If the first fever cure is not followed by improvement, there is no hope that a second cure, carried out sooner or later after the first, will be more successful. In cases of incomplete remission after the first cure, a second is indicated whenever the patient shows the first signs of relapsing into the state prior to the treatment. Repeated treatment is also advisable in patients with partial remissions after the first cure, even though there are no evidences of recidivism. According to Schwarz, the second series of treatments gives the best results when it is carried out at an interval of from one-half to one year after the first. If the patient responds to the first cure by remission, he should be submitted to a second one as soon as he shows signs of recrudescence of the disease. On the whole, the second fever treatments proved to be markedly less successful than the first ones.

The course of juvenile dementia paralytica following malaria therapy is the subject of a paper by Heinze. His material comprised 32 patients, from 5 to 22 years of age. In 2 cases the inoculation with tertian malaria did not cause a rise in temperature. Favorable results were obtained in 27.9 per cent of the 32 cases. While the percentage is relatively low and the remissions are not as good as those which he obtained in adults. Heinze finds his results encouraging, considering that no other therapeutic procedure is known to be of any value in the treatment of juvenile dementia paralytica.

Roggenbau favors the use of a nonspecific protein in combination with arsphenamine and bismuth. He considers that nonspecific proteinotherapy or any chemical substance capable of inducing fever activates organic function and immunizing processes similarly to malaria inoculation. He also records his experience in attempting to treat dementia paralytica by specific active immunization. Ten patients with dementia paralytica received subcutaneous injections of a suspension showing from 3 to 5 living spirochetes in a dark field. The injections were repeated at intervals of fourteen days, the total number ranging between eight and twenty-five. Of the 10 patients treated, Roggenbau noted moderate remission in 3, no change in 2, a progressive decline in 3 and death in 2.

Warstadt discusses the paranoid-hallucinatory condition in patients with dementia paralytica following fever therapy. His extensive review of bibliographic data does not lend itself to a concise abstract.

Bender describes the postmortem findings in 30 patients whose death either was caused by the malaria treatment or occurred shortly after it. Pneumonia was the predominant cause of death. A definite relationship could be established between the gravity of the clinical symptoms and the histopathologic changes in the brain. No parallelism was noted, however, between similar clinical phenomena in various persons, on the one hand, and the nature, intensity and localization of the structural alterations on the other. There was no evidence of transformation of chronic dementia paralytic processes into a state of acute syphilitic encephalitis.

An interesting study of the social adjustment of patients with dementia paralytica who had had the malaria treatment was made by Kathe Misch-Frankl. Eight hundred patients were investigated. Of these, 23 per cent had regular occupations, and around 30 per cent were unable to support themselves; 6.5 per cent had insurance compensation; 17.5 per cent received support from social sources, and 6.2 per cent from private sources. About 6 per cent were idle, not because of inaptitude for work but on account of the general economic condition. Including these unemployed, the number of patients who preserved their working capacity equaled the number of the socially useless patients.

The last paper in this volume, by Fritz Mollenhoff, discusses the topic of malaria therapy and the social standing of patients. The latter are inmates of a private

sanatorium, i. e., persons of relatively higher economic status. The clinical material, as the author states, is, however, small, and the discussion is chiefly based on bibliographic references.

On the whole, this volume of collected papers is highly commendable. It offers the reader a comprehensive review of the actual state of knowledge on fever therapy in general and of malaria therapy in particular.

Apparatus for the Rapid Study of Ultra-Violet Absorption Spectra. Special Report Series, no. 177. Price, 1 shilling, 3 pence. Pp. 45. London: His Majesty's Stationery Office, 1933.

This report by the Medical Research Council describes new methods of physical investigation by members of the staff of the Medical Research Council at the National Institute for Medical Research, at Hampstead.

The use of ultraviolet absorption spectra for the analysis of mixtures of chemical substances in solution played an important part in the studies of the nature of vitamin D during which it was necessary to examine mixtures of substances having closely related or similar absorption spectra. Rapidity as well as accuracy was an essential requirement in this work, because a large number of spectroscopic measurements had to be made within the narrow time limits allowed by the instability of the substances under examination. By this method a complete absorption curve may be obtained for a given organic substance if it remains unchanged for only five seconds.

The authors consider the four necessary instruments in detail. First, the spectrograph, its optical system and construction, is discussed. The second is the densitometer, with its optical system and microscopy. The photometrograph, by which the readings of the densitometer were converted into basic units and plotted on a graph, at a speed comparable with that at which they were obtained, is next discussed. The last is the mixigraph, a wooden framework arranged with a fixed 100 division scale and with four metal fittings each provided with a small hole into each of which black threads are anchored. Two guide rods are mounted parallel to the right of the scale. Arrangements are made by springs to keep these threads fairly tight at all times. By means of the mixigraph, graphs can be plotted at the rate of six points per minute—whether the absorption curve of a mixture, given those of the two components, or the absorption curve of one component, given those of the other component and of the mixture. Further, graphs can be replotted from the original to either a larger or a smaller scale of ordinates.

The entire apparatus is based on a photographic photo-electric method. It is rapid in effect because it provides measurements at all wavelengths from one spectrogram of the solution and of one of the solvents, and the adjustments for measuring at a series of wavelengths are fewer and simpler than are most direct photo-electric methods. The system is also fairly satisfactory as regards error, for various reasons which the investigators describe in more or less detail. The greatest sources of error possible are those of the photographic plates. While many of the errors in a photographic plate were eliminated so far as the results were concerned, certain others remained which had to be considered.

The authors believe that with the densitometer and photometrographic apparatus they can obtain better results than with direct spectrophotometric practices. While with their method, measurements cannot be made until the day after photography, this disadvantage, as compared with the direct photo-electric method, is offset by the fact that a substance need remain unchanged only for five seconds in order to provide a complete absorption curve representing its condition during that period. This is important if the substance is chemically or photochemically labile. Another advantage is that during a complicated experiment large numbers of spectrograms can be taken, the measurements being made later.

The apparatus worked out by these investigators and their method of studying ultraviolet absorption spectrophotometry comprise a most valuable addition to the laboratory methods at present available.

Anjea. By Herbert Aptekar. Price, $2.50. Pp. 192. New York: William Godwin, 1931.

Anjea is a monstrous blackfellow made by Thunder, who fashions black babies out of swamp mud and puts them at his will into the wombs of women; under this title Mr. Aptekar in this book, which deals with infanticide, abortion and contraception in primitive society, maintains as his thesis that the general civilized attitude, whether favorable or unfavorable toward birth control, is as naive, mythological and primitive as that of the Australian blackfellow. As an approach to the problem he raises the following questions: Is this form of social behavior common to all mankind? Has it always existed? Does it have the same meaning everywhere; i. e., does one always find the same psychologic relation to it? What part does reflective thinking play as a factor conditioning voluntary restriction of numbers? How do the various uses so unified conceptually act on the phases of life and cultural growth, and on the growth and decline of population? How do other forms of behavior act on these uses in differing societies? In short, does there seem to be any generally valid societal law applicable to this aspect of life?

In his first chapter, "The Desire for Progeny," Aptekar points out from a review of this question in various cultures and societies that the desire for and to avoid children depends in any society on: (1) Two constant factors inhering in the parent-child relationship: (*a*) the joy of children—associated with the positive desire; (*b*) the burden of children—associated with the negative desire. (2) Specifically cultural components of these desires varying in disparate cultures. (3) Historical as well as psychologic determinants of both desires. (4) The continuity of both desires and the remainder of culture.

In the third chapter he shows that the practice of contraceptive measures is not based on malthusian expediency, but is undertaken for a great variety of reasons in different societies and cultures. Chapters 5, 6 and 7 deal with contraceptive practices, abortion and infanticide among primitive peoples.

The author concludes that practice tending to the restriction of progeny are almost universal and have always existed. In answer to his other questions he points out that no general rules can be formulated because contraceptive practices are not isolated entities but are part of the general culture and behavior, and so can be evaluated only in relation to this. The book is of interest in that it attempts to take the question of contraception out of the field of controversy and consider it in a scientific manner as a form of human behavior.

Probation and Criminal Justice. By Sheldon Glueck. Price, $3. Pp. 344. New York: The Macmillan Company, 1933.

The use of probation in the treatment of crime is one of the most important fields where psychiatry and social science find a common ground. It is therefore highly desirable that psychiatrists acquire some familiarity with the whole problem of probation, which seems destined to play an increasingly large rôle in the administration of justice.

The present volume, edited by Sheldon Glueck, is an admirable introduction covering the whole field in broad outline. Most of the aspects of probation are covered in separate chapters written by specialists. All angles of the problem are considered—legal, administrative, judicial, technical, organizational and historical. The editor himself contributes an informative and well balanced introductory chapter. Judge Ulman of Baltimore writes a humanly appealing chapter on the trial judge's dilemma, showing the struggle in a judge's mind between common sense and legal tradition. Dr. Bernard Glueck covers the psychiatric aspect of probation entirely from the psychoanalytic point of view. There are chapters on probation in England, France (which has no probation for adults), Belgium and Germany (where the chief protagonists of an enlightened probation policy have just been ousted). A chapter on Russia, where the most important advances are made at the present time, is lacking.

There are a good index of subjects and names, informative footnotes and good bibliographic references. This book can be thoroughly recommended as an introduction to the subject.

The Approach to the Parent (A Study in Social Treatment). By Esther Heath. Price, $1.25. Pp. 184. New York: Commonwealth Fund, 1933.

The interest in this book lies in the fact that Miss Heath, through four of her own cases carried over a period of eight years, traces the changing philosophy of her own thinking. In general, one can agree with her premise that objective case work implies that the social worker have a good understanding of herself so that her work may be a working out of the client's difficulties rather than the development of a relationship which meets the emotional needs of the social worker. Her cases, too, illustrate nicely the service a trained person can give in smoothing out environmental difficulties which are contributing factors to a child's maladjustment. The freudian school might well take issue with her on her conception of the passive approach since, in the cases she gives, the social worker seems to furnish the solution and looks to the client to live up to her expectations. For example, in case 4 the worker appears to expect the client to develop parental love for a much rejected child. Her concern about fostering dependency in this case might make one wonder if it prevented her from making the most constructive use of the client-worker relationship to guide the mother to make her own decision. In all the cases there is considerable emphasis on developing parental love, even in cases in which the underlying causes of the parent's hostility are recognized.

The second and third studies illustrate admirably ones in which parental love is not heavily overladen with antagonism based on deep emotional conflict. Both of these cases are well worth reading because of the graphic way in which the author portrays the technic she has utilized to give the parents a better understanding of a child and through the child has helped the mothers to gain a better understanding of themselves.

The book as a whole illustrates nicely one of the present-day approaches and points of view of the social service field.

Die Prohibition in den Vereinigen Staaten. By Dr. Günter Schmölders. Volume 8. Forschungen zur Völkerpsychologie und Soziologie. Price, 7.50 marks. Pp. 266. Leipzig: C. L. Hirschfeld, 1930.

This painstaking and objective study of the motives and effects of the American experiment is a volume of the researches of folk psychology and sociology published by Thurnwald. In keeping with the standard of this well known investigator, the author gives the evolution of the movement and the history of the legislation and the resulting methods and statistics in an unbiased and dependable presentation, to the beginning of the now completed repeal legislation. The book stands in great contrast to the purely polemic pamphlet of Mendelsohn.